

3. In cases in which hemorrhage might cease and a laparotomy be not needed, the procedure would be of the greatest value. Apart from combating shock, the solution would mingle intimately with the blood, hold the particles in suspension and hasten absorption of the fluids in the peritoneal cavity without allowing coagula to form, to be the foundation of troublesome and perhaps fatal adhesions and strangulations.

4. The procedure would not require great skill, but would be feasible in the hands of any general practitioner. The following is offered as a suggestion: The solution should be kept sterile in a flask, fitted in a portable case, which could also contain a compartment for a small bottle of alcohol, in which to keep the trocar sterile and ready for use, and another to accommodate a long sterile rubber tube to serve as a connection between the flask and canula. Then in case of emergency the solution could be quickly raised to the required temperature, a small area of skin sterilized, the trocar introduced and the diagnosis made, the flask and canula connected and, by raising and lowering the flask, the flow could be regulated and the amount noted. After a gentle flushing of the peritoneal cavity, 500 c.c. to 1,000 c.c. might be kept within and the patient sent to the hospital, the better prepared for later developments.

#### DISCUSSION.

DR. WINFIELD S. HALL, Chicago, in reply to questions, said that no leucocyte count was taken during these experiments. The hemorrhages were produced thus: A small incision was made and one of the branches of the mesentery artery cut through this incision and allowed to bleed until the intravisceral spaces were partly or wholly filled, and then the wound was closed. There is no way of determining the exact amount of hemorrhage without drawing it off in some vessel and then putting it back. Dr. Hall said that it was not thought desirable to depart so far from what would be found in ordinary cases. Some observers have withdrawn blood and defibrinated it.

DR. S. J. MELTZER said that he believed that if the bleeding comes from a small artery the best plan is to leave it alone, since the contraction of the vessel wall in conjunction with the clotting will soon stop the bleeding, aided especially by the intra-abdominal pressure. Bleeding from large vessels can be stopped only by ligature after laparotomy has been made. If, however, the bleeding comes from the parenchyma of a ruptured organ, a transfusion of saline can do only harm, since it would tend to increase the blood pressure and with it the bleeding. Transfusion can be useful only after the bleeding has stopped, to supplant the lost blood, but can hardly be employed for the purpose of stopping the bleeding.

DR. V. C. VAUGHAN, Ann Arbor, Mich., said it is the consensus of opinion that it is bad to inject salt solution or anything else when there is a possibility of infection. The abdominal cavity is divided into departments. If solution is used it carries the infection. For this reason surgeons are giving up the washing out of the cavity. It spreads the infection and carries it to every part of the intestine and makes the surface on which the germs grow much larger. Those who do not wash out the cavity certainly have the best of the argument.

DR. WINFIELD S. HALL, Chicago, said that an artery was chosen for the experiments because of difficulty in controlling the hemorrhage while getting the amount of blood wanted from the spleen or liver. There were fifteen dogs; eight had saline solution and seven did not. Those that did not have the saline solution had a considerable rise in temperature. In the case of the dogs that had it there was no evidence of temperature. The wounds were opened up to see the progress of recovery. In several cases in which no saline solution was used clots formed which made it very evident that the course of recovery would yield to adhesion that might cause strangulation. In no case in which saline solution was introduced was

anything of that kind shown. So far as appearance goes, the experiments left no doubt but that saline solution was of great value. As Professor Vaughan pointed out when there was a rupture of the intestine with danger of spreading the infection, this would be bad procedure.

DR. S. J. MELTZER, New York, asked what was the cause of the difference when no saline solution was used.

DR. WINFIELD S. HALL said that there was one case in which sepsis had miscarried and in that case there was some temperature. In other cases he could account for the increase of temperature only as due to the action of the peritoneum. There was no infection. It may have been due to absorption of the clot. He usually associates it with infection, but there did not seem to be any infection.

## OBSERVATIONS ON THE FUNCTIONS OF THE ASSOCIATION AREAS (CEREBRUM) IN MONKEYS.\*

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Our knowledge of the functions of the cerebrum has been obtained from studies of the effects of stimulation and destruction of the various parts of the organ. In this study both physiologists and clinicians have been engaged. Physiologists have spent most time in determining the effects of lesions, experimentally produced, and the motor accompaniments of stimuli of different kinds. The clinicians, including surgeons, neurologists and pathologists, have been able to observe in man the effects of destructions from accidents, disturbances of functions from emboli, thrombi and hemorrhages, and in some cases it has been found practicable to stimulate the cerebral cortex in man after the fashion of the physiologic experiments and thus to map out the muscular reactions represented in the cortex.

#### PHYSIOLOGIC AND CLINICAL METHODS.

Both the physiologic and the clinical methods have advantages and disadvantages. On animals the physiologist is enabled to limit the lesion, to repeat his experiments often and to make detailed observations on individual points, to use any or all the apparatus of a laboratory and to observe his "patients" before and after an experimental accident. The clinician, who is dependent on "Nature's experiments," is limited in some of these directions, but on the other hand he has a great advantage in that he deals with men. From the responses of a patient one can learn more of his feelings, of his sensations and of his other mental states than is possible with animals, and the lack or disturbances of speech ability which are found in some individuals are of more value for the understanding of certain cortical functions than hundreds of experiments on dogs or cats or monkeys. The two methods, it is well understood, supplement each other, and the student of brain functions must consider and weigh the results of both.

Both methods have been most successful in the determination of the motor and of the sensory functions of the cerebrum. The physiologists have been unable to advance our knowledge of the workings of the so-called association areas represented by over one-half of the

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\*The present paper is in the nature of a preliminary communication. A full account of the experiments which were made will be published soon. The work on monkeys was made possible by a grant from the Carnegie Institution of Washington to the author.

cerebral cortex. These portions of the brain do not produce a motor response on stimulation, and the effects of destructions or extirpations are not worked out. On the other hand, in only one particular have the clinicians been able to demonstrate clearly the functions of any of these parts, viz., in the localization of the functions of speech. The relative importance of the frontal or the parieto-occipital association areas in mental states has been often considered and the conclusions have been totally different. The more recent attempts have been to locate "mind," or the "higher intellectual faculties" in the frontal region, more especially in the prefrontal lobes.

In this country Phelps<sup>1</sup> and Mills<sup>2</sup> have championed the cause of the frontal lobes, particularly the left, as the seat of "thought." This has been done, it seems to me, without a sufficient analysis of the mental symptoms associated with cerebral injuries and without careful studies of the brains of individuals with high and low mental development. On this latter point it may be mentioned that the brains of Gauss and Helmholtz, which have been considered by Mills to indicate the predominant importance of the frontal lobes in intellectual states, are described by Clapham<sup>3</sup> as examples of great complexity of convolution in the zone between the Rolandic and the visual areas. Clapham, consequently, considers this region to be particularly associated with high mental development. The cases cited by Mills and those given in Schuster's admirable book,<sup>4</sup> which bear on the subject of the functions of the associational areas, I shall consider in detail in another article.

#### PHELPS' WORK.

There is time now to take up only very briefly some of Phelps' cases and conclusions. This I shall do in support of my previous statement that the conclusions regarding the functions of the frontal lobes have been drawn without a sufficiently careful analysis of the mental conditions in the cases of cerebral injury. "Loss of consciousness, the event of stupor or the access of delirium have been found to be dependent on the nature of the lesion, apparently uninfluenced by its situation," is a general justifiable deduction made by Phelps from all his cases.<sup>5</sup> From the results of his frontal-lobe cases the following conclusions are drawn:<sup>6</sup>

1. Mental decadence always attends conjoint lesions of both prefrontal regions. 2. Mental decadence always attends lesion of the left prefrontal region alone. 3. Mental decadence never attends lesion of the right prefrontal region alone.

The cases of frontal laceration cited in his book and the sixteen cases in his article do not admit such broad inferences. Of the eleven cases of laceration of the left frontal lobe only Cases 6 and 9 were undoubtedly conscious and without stupor or delirium, but with a mental change. Ten cases of laceration of both frontals (pp. 130-131) include four patients in whom the mental condition was "normal" on days following the injury, and Case 300 (p. 580) is probably an example of mental impairment with lesion of the right frontal lobe. It is unfortunate that all of the individuals with lesions in the left frontal alone, or in both frontals, whose cases are given in Phelps' recent article, died soon after the

accidents. We can see, however, that not all individuals had their mental faculties located in the left frontal lobe. The patient in Case 2 with a left frontal lesion comprehended up to the morning of his death. The patient in Case 3, although there was a certain amount of stupor and fever coincident with the left frontal injury, could be roused sufficiently to answer questions, and when the fever had only partially subsided the "comprehension was less delayed." In Case B, a fall on the right side, the patient showed a mental defect for at least two weeks. In Case C patient was discharged on the twenty-second day with delusion persisting after injury to the right side of the head. In Case D, a fracture on the left side, patient was entirely rational at the end of the fourth week. I am well aware that the cerebral lesions in the last three cases were not determined, but we are as certain that the brain injury in Cases B and C was on the right side as that it was on the left in Case D.

From a psychologic standpoint, what is lacking in all the accounts is a careful analysis of the mental condition. Apathetic, dull, stolid, irritable, restless, nervous, deficient memory, slow comprehension, are general terms for conditions which, for scientific purposes and in the present stage of psychology, the observer could and should try to describe more carefully. Any one of these terms may be descriptive of states of deficient or wandering attention, some are indicative of a mild degree of delirium. It is of prime importance that every case should be examined from a psychologic standpoint, if psychologic inferences are to be drawn.

A similar criticism must be made regarding the conclusions of most physiologists in regard to the functions of the association areas. The observations which they have made are even more "casual" than the clinical ones. Loeb<sup>7</sup> says that it is "impossible to notice the slightest difference in the mental functions of the dog" if both frontal lobes are removed, although he does note that if the anterior halves of both hemispheres be removed an animal becomes "idiotic." Such a careful observer as Schäfer<sup>8</sup> uses the term "semi-idioty" to describe the mental condition in monkeys following the removal of the temporal lobes. Idioty in children is difficult to diagnose from simple observation and the term "semi-idioty" has no meaning in psychologic practice.

For the reason that the description of results of previous physiologic work on the association areas was lacking in exactness and definiteness, about six years ago I devised a method to determine more accurately the functions of these parts in animals. The mental life of animals, and even of man, is made up very largely of series of association, which in general terms are of a simple sensory-motor character.<sup>9</sup> Any definite sensory-motor association may be produced in an animal in a very few days, and it is possible to discover whether or not the association persists after removal of parts of the cerebrum.

#### AUTHOR'S EXPERIMENTS ON CATS.

The results of an investigation of this character, viz., on the relation of the frontal lobes to the production and retention of simple sensory-motor habits in cats, have

1. "Traumatic Injuries of the Brain," second edition, 1900; also articles in the *New York Med. Jour.*, 1894-5, and *Jour. Med. Sci.*, 1902, 1906.

2. Mills and Weisenburg: "Localization of the Higher Psychic Functions," *THE JOURNAL A. M. A.*, 1906, vol. xvi, p. 337.

3. *Jour. Ment. Sci.*, 1898, vol. xiv, p. 290.

4. "Psychische Störungen bei Hirntumoren," 1902.

5. "Traumatic Injuries to the Brain," p. 127.

6. *Am. Jour. Med. Sci.*, vol. cxxxi, p. 457.

7. "Comparative Physiology of the Brain," p. 275.

8. "Text-book of Physiology."

9. For an account of animal psychology and the mental life of animals the reader is referred to the works of Thorndike, Lloyd Morgan and Hobhouse.

already been published.<sup>10</sup> In that article the method is described in full. I may paraphrase briefly:

An animal is placed in a certain environment, usually unpleasant or indifferent to the animal. By a simple motor adjustment the cat or the dog or the monkey gets a subsequent pleasure (for example, some food). At first the motor response is neither accurate nor speedy, but soon the animal learns—i. e., forms the association of a definite movement or set of movements with a given situation. When the association or habit is "set," it is possible to discover that portions of the cerebrum are concerned in its production or retention by the extirpation of definite regions and the determination of the presence or absence of the association. If, after the destruction of a part of an animal's brain, there is no alteration in its mental condition, the time for the production of a movement or set of movements, when the animal is placed in a situation calling for such motor response, should remain the same. It was found, however, that after a bilateral lesion in the frontal lobes certain habits were lost. This result, it was shown, could not be due to "shock," for other brain lesions were not followed by loss of such associations. Unilateral lesions in the frontal areas were followed by a slowing of the motor response.

#### AUTHOR'S EXPERIMENTS ON MONKEYS.

Some similar and some totally negative results from similar experiments have been obtained with monkeys by me since the publication of the experiments on cats. These I wish to report at this time. The simple associations which I produced in the monkeys are what may be called "food box" and "hurdles."

*The Food-Box Experiment.*—In the food-box experiment the animal was placed in a small cage, about eighteen inches cube, which was covered with wire netting and to which was attached at the back, in the upper right-hand corner, a smaller "food box" about seven inches cube. The door of the food box was fastened by an old-fashioned turn-button, which had to be turned through an angle of 90 degrees before the door of the box could be opened. A greater or less turn would keep the door of the box closed. The button of the food box was placed sufficiently high, so that the animal had to stand and reach for it. A hungry animal was placed in the small cage, food was put in the box and the animal attempted to get at the food. When the animal was first placed in the peculiar situation it made many random movements, trying to squeeze through the wire netting, shaking the door and putting its hands all over the box and the cage. In its random movements the button may be turned and the door of the box come open. The animal sees the food, takes it and eats. After a very few trials the attention of the animal is almost exclusively centered on the food box and its door, and so soon as the food is placed in a box it will immediately turn the button. The association has been formed. This association will persist for a long period, two to three months, without materially altering the average time for the performance of the complex act.

*The Hurdle Experiment.*—The "hurdle" gave a situation a little more complicated. The animal was placed on a box ten inches high, from which it jumped or walked to a bar fifteen inches high, thence to another bar ten inches high, through a hole six inches in diameter, in a box six inches deep, then up and down two short ladders placed together, and finally it lifted the lid of the middle one of three boxes in which it found some food. The "hurdle" or obstacle race is much simpler than the description would indicate; its complexity is rather at the end in the choice of the proper (i. e., the center) box for food.

When an animal had learned the "hurdle" or "food box," of both, it was put aside for a week or ten days, with no practice, and then its memory was tested. A few extra trials to get the habit well learned were given and then the frontal lobes were cut away from the rest of the cerebrum. The surgical procedure was the same as I had previously used with cats.<sup>11</sup> Nine monkeys learned one or both of the associations and survived the operation for a sufficient length of time to have their memories tested. Some lived over nine months. Seven of the animals were of the macaque family, two were ringtails.

#### RESULTS.

The final results of the experiments I may group in three general divisions:

A. This class consists of two monkeys; both lost their newly-formed habits after the removal of the frontal lobes. The tests of retentiveness in these cases were made, respectively, about 24 and 40 hours after the operations. The results were very decided. Neither of the animals moved toward the door of the food box, but made random movements about the cage. One of the animals was restless, the other was stolid and indifferent. Each lived only a very few days (three and five, respectively). The autopsies showed that the frontal portions had been cut away from the rest of the cerebrum, but there was in one case an increase in intracranial pressure which was evidenced by a bulging of the brain substance when the bandage and trephine buttons were taken off. The results in these cases are in themselves of little value for the drawing of conclusions, it seems to me, because the animals survived the brain lesions for only a short time. It should be remarked, however, that the interval between the operation and death in both cases is as long as between accident and death in man in many cases which the clinicians report and which are highly rated.

B. The second class consists of three animals, a rhesus monkey and two ringtails, who lost their newly-formed associations after the removal of the frontals. All these animals lived a sufficiently long time to determine that the loss of habits was not due to the primary shock effects of the operation on the brain, but was a loss of the sensory-motor associations. The rhesus monkey died from hemorrhages subsequent to a second operation three months after the first operation. During the interval between the first and second operations the animal seemed perfectly normal (with the exception that the "food-box" and "hurdle" habits were lost), and when with other animals in a large cage it was impossible to note any difference in its behavior. This animal in the months following the first operation relearned the "food-box" association and the second operation was performed to determine what portion of the brain was concerned in the production of the habit after the prefrontals were excised. In cats I found that it was possible to teach an animal a trick, to remove the prefrontals and find the habit lost; then to have the animal relearn the same trick and to have it lost after removal of more of the frontals; and in the same manner for a third time to have an association formed and to have it lost subsequent to a third operation. It is possible, therefore, to have a mental defect, but to have a recovery in animals within a very short time, by a proc-

10. Am. Jour. Physiology, 1902, vol. viii, p. 1.

11. Am. Jour. Physiology, 1902, vol. viii, p. 5.

ess of relearning. A similar recovery has been obtained in the event of disturbance, or even of destruction, of the speech centers in man.

The other two animals that showed a loss of associations after the removal of the frontals lived, respectively, six and two months. Both of these ringtails had learned to jump from a shelf to my shoulder when I snapped my fingers, and this habit was lost as well as the "hurdle" and "food-box." Subsequent to the operation both of these animals seemed less friendly, they chattered more and screamed and showed their teeth when another monkey or a person approached them. In other respects their behavior was normal.

C. In my article on the effects following lesions of the frontal lobes in cats<sup>12</sup> I pointed out that habits, i. e., associations, of long standing were not lost after destruction of the prefrontal regions. A similar result was found with four monkeys in the present research. The associations which were investigated were mainly those of the "food-box." The most important of these cases is that of a female rhesus, living at the present time, two months after the operation, which was practiced on the "food-box" for 27 days, 5 times a day, over a period of 234 days. This animal learned to open the door of the "food-box" in an average time of 1.1 sec. before the operation, and two days after the operation the average time of 10 experiments was found to be 1.8 sec. At the middle of the tests with this monkey a period of 160 days was left free from any practice on the "food-box," and after this long interval the memory for the performance of the appropriate movements was perfect; average time before interval, 3.8 sec.; average time after interval, 4.4 sec. In this monkey the motor response partook of the nature of a reflex, and it is possible that the cerebral cortex was no longer used for the sensory and motor association, but that the adjustment was made in the basal ganglia. Probably a similar process in man of the assumption by lower centers of activities which at first are carried on by the higher is to be found in the learning of games, etc.

A male rhesus who was practiced 18 days over a total period of 43 days showed, so far as the ability to perform his "tricks" was concerned, no effect after the removal of both frontals. Another animal, a macaque, was trained for 15 days, and after operation his ability measured by the average time to perform tricks was lessened. Before the destruction of the frontal lobes he averaged 1.8 sec. for opening the "food box;" after the operation and for a few days his time was greatly lengthened, e. g., on the second day it averaged 23 sec. The fourth monkey which did not lose its habits after the removal of the frontal lobes also showed a retardation. In this animal the slowing was, however, not so marked as in the previous case.

#### CONCLUSIONS.

Conclusions to be drawn from the experiments may be summed up as follows:

1. In monkeys, as well as in cats, the frontal lobes are normally employed in the formation of simple sensory associations.

2. When the frontal lobes are destroyed, recently formed habits are lost. It has been found possible, however, for the animal to form new associations or to relearn old tricks.

3. When the associations are firmly established, destruction of the frontals is not always followed by a loss.

There are all degrees of "memory" for any such particular habit, from perfect to a very decided hesitancy and slowing.

4. In this latter event the cerebral path is probably shortened, and the nervous connection of the sensory and the motor elements of the association takes place through tracts at the brain stem. The association has, therefore, more of the character of a reflex.

In addition to their value in indicating the functions of part of the associational areas in monkeys the results, I think, have a suggestive import for workers on the pathology of the brain of man. The experiments show not only that there are mental changes coincident with disturbances of the frontal lobes, but that the mental change which is described is one that could not be determined by simple observational methods, and they suggest, furthermore, that, for the determination of corresponding changes in man, accurate psychologic or psychophysical methods should be employed. The clinical, as well as the physiologic, evidence points to a dependence of certain mental processes on the integrity of the frontal lobes, and I am much inclined to believe that the frontal or prefrontal areas are of great value in our mental life. I feel, however, that the reported clinical observations do not prove this and that there is great need for more careful psychologic examination and experiment in the hospitals. The weakness of the clinical work is that so much is claimed without an adequate analysis of the mental conditions of the patients.

Much more and better information could be gathered if the patients were tested along the lines which are followed in psychologic laboratories and psychiatric hospitals. In any scientific work there can not be too great accuracy either in methods or in results. This is particularly true when the subject of research is so elusive a thing as is "mind." Careful dissection, sectioning and the use of good microscopes are deemed necessary in other fields of medical work, and psychologic scalpels, microtomes and high power lenses are indispensable to one who would attempt to solve the problem of the relation of the brain to mental processes.

#### FURTHER OBSERVATIONS ON THE INFLUENCE OF ALCOHOL ON THE METABOLISM OF HEPATIC GLYCOGEN.\*

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The present report gives the results of a further study of the possible influence of alcohol on the metabolism of glycogen in the liver. It has recently been shown that, to a certain extent, alcohol can replace the carbohydrates of our daily diet. Consequently it would seem *a priori* that it might indirectly be a glycogen former, by sparing the carbohydrate radical of the tissue proteins, which may serve as a source of glycogen. The results of Nebelthan's<sup>1</sup> investigations, indeed, lend some support to this view. He found considerable quantities of glycogen in the liver of the hens to which large amounts of alcohol were fed after they had been starved for six days. In one of his experiments he found as

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1. Nebelthan: *Ztschr. f. Biol.*, 1891, vol. xxviii, p. 138.

12. *Am. Jour. Physiology*, 1902, vol. viii, p. 22.