

Dr. W. Ross Adey: I hope to devote the 25 minutes that I am allotted to the pursuit of two main aspects of this problem of behavioral neurophysiology. One will be the elucidation of techniques and methods that have grown up rather as a specialty out of the classical morphological anatomy and the classical neurophysiology of the last 20 years to represent in essence a new discipline in the examination of functions of the brain. What I hope to show is the very basic way in which we, who perhaps have less imagination than most people, go about these things. I think Dr. Pribram will show how the erudite psychologist can achieve new theories from this material.

It is not necessary for me to tell this audience what happens if, for instance, one takes out the temporal lobe of the brain on both sides. Dr. Bucy and Dr. Klüver examined this syndrome 20 years ago in Chicago. Dr. Klüver coined the term "psychic blindness" to describe the animal's condition with tameness, hypersexuality, oral tendencies and altered social behavior as the main manifestations of the disease or the syndrome. One can achieve in essence a dissection of parts of this picture by making more limited ablations than those that characterize the Klüver-Bucy syndrome.

This first slide shows what happens if, for instance, one removes the amygdala in the cat, leading to typical aspects of hypersexual behavior. Here a cat attempts intercourse with a dog, here with a chicken, and here with a monkey, and here four cats are engaged in the delicate occupation of what is called tandem copulation. This work by Dr. Schreiner and Kling in Washington some years ago was, I think, epitomized by the efforts of the monkey to have intercourse with a white mouse, with the inevitable result that there was a lesion of the glans penis.

A less exciting dissection of the picture is possible and is exemplified by the findings that certain aspects of altered behavior are universal through the scale of mammals following restricted lesions of the temporal lobe.

If, for instance, one removes the pyriform or entorhinal cortex in the temporal lobe, leaving intact the hippocampus and the amygdala, one finds a picture of extreme tameness in an animal that is otherwise savage. For instance, the Australian marsupial phalanger ordinarily is herbivorous but very savage. After removal of the cortex, one can handle it like a domestic cat, and it is a quite pleasant animal.

Likewise, if one removes a comparable area of cortex in the baboon, leaving intact the hippocampus and amygdala, one finds the animal considerably tamed. Postoperatively, these baboons were trained to press a lever for a reward of candy. They were trained further to avoid contact with the lever when a light cue appeared over the lever. The normal animal became extremely frustrated in this situation, whereas the animals operated upon showed almost no responses of rage under the same conditions. This would appear to be an aspect of altered behavior at a fairly high level.

Let's discuss briefly the question of mechanisms that might be involved. Twenty-three years ago, Dr. Papez described "a proposed mechanism of emotion" involving the hippocampal structures, on the basis of a circuit running from the hippocampus through the fornix to the hypothalamic areas, then to the thalamus and cingulate cortex, around the cingulate arch to the hippocampal gyrus. So one had a pathway from the hippocampal gyrus to the hippocampus, with anteriorly directed activity running in the fornix toward the hypothalamus.

Here is an interesting concept. It shows something that made us stop and wonder whether in fact this was the main stream of activity between the hippocampal structures and the hypothalamus as a basic functional interrelationship. This diagram is one that is almost a dirty word, I guess, with many people, showing the existence of a reticular core to the brain stem, with activation of this core from the various peripheral inputs and
relays to the cortical surface in a "nonspecific" fashion and thus constituting the ascending reticular system. This system is said to be responsible for behavioral arousal through its ascending cortical connections, but it is necessary to remember that the reticular core is played upon by a series of descending influences which pass into it from a wide variety of cortical areas, and especially from the basal temporal cortex, including the entorhinal area and, as we shall see later, from the amygdala anteriorly.

Now, I want to deal for the rest of this discussion with the interrelations between this cortex and the brain-stem core, since we believe many aspects of these behavioral processes are manifested through such a mechanism.

Here is the Papez circuit from hippocampus to hypothalamus, with activity directed into the cingulate cortex through the thalamus and ultimately returning to the hippocampus again. But we are going to talk about a circuit that, as a result of our physiological investigations, appears to be rather more important; namely, one in which the reticular substance activates the septum and the septum in turn sends activity back promptly through the fornix to the hippocampus and the entorhinal area in the opposite direction to that suggested by Papez.

If one examines this series of pathways in more detail, the suggestion is that septal activity comes back through the fornix to the dentate fascia, thence to the hippocampal pyramidal cells, and so to the pyriform cortex. One might regard this arrangement as a set of concentric shells, the dentate being the innermost, the hippocampal pyramidal cells the middle layer, and the pyriform cortex the outermost. We have reason to think that there are powerful projections from this entorhinal or pyriform cortex into the tegmentum lateral to the periaqueductal gray matter, perhaps partly involving the periaqueductal gray matter itself. This is the series of mechanisms we have investigated from the behavioral point of view in a variety of animals.

The technique that has proved very fascinating is the use of freely moving animals with implanted electrodes in their heads. They may wander around while we record the electrical activity. We may administer drugs to them and in a variety of ways manipulate their behavior.

We have in some 30 cats over the last 2 years placed implants in the dorsal hippocampus, in the ventral hippocampus and the entorhinal area, and in the amygdala.

Here is an animal with a series of such implants in one of our typical tests. It is a T-maze box, a large box where the animal is behind doors which here are opened, and at this stage the animal is coming down the box to a reward of food on the basis of a light fixed above the food. Here is a partition which divides the box into left and right halves. You can see the cable that connects the animal to the recording amplifiers. We have been at great pains to develop techniques in which these records are possible without the artefacts of movement that are so common in taking electroencephalograms in freely moving heads of humans as well as animals.

Here are a series of electroencephalographic records, all taken from the hippocampus or entorhinal cortex, when the animal is completely naive. This is the first time it has been in the box and this is his second run down the box. You can see here the doors are open. The animal advances, looks at the light and steps up, and here it eats the food. In this second trial there obviously are very regular rhythmic trains of waves at about 6/sec. in this series of cortical structures, and they are synchronous in many parts of the hippocampus.

By the time the animal has run 20 times on this first day, much of this rhythmic activity from the ventral hippocampus is now a residual and essentially a permanent phenomenon in the entorhinal cortex. Thus we have here something that is labile in the behavioral situation. If it is a situation completely novel to the animal, then it will last or it is more widely distributed. It is redistributed after the first few trials to the dorsal hippocampus and the adjacent pyriform or entorhinal cortex.

Let us look at these movie frames of the animal as it runs, and at the simultaneous electroencephalographic records. Here is the animal in the start box with doors closed and the doors are opened in frame 2. Its head is appearing and it is starting to run. It moves down the box. It is almost at the goal. In the fifth frame it has reached the goal. If we look at only one lead, we see here during the approach to the goal, in the entorhinal cortex, a very regular rhythmic series of waves that are actually \( \frac{3}{4} \) c./sec., and this will persist throughout the animal's training to perform the correct response.

Here is an example in which the animal in the first instance goes to the wrong side of the box, later corrects and goes to the right, and in the approach to the goal there is a burst of this \( 6 \) c./sec. activity and again here a second burst of it as the animal reaches the goal.

I realize these records look a little, shall we say, scratchy. This is because we are anxious not to restrict the band pass of the electrical information. If we had restricted it, it would look nice and clean; but for the purposes of the analysis of the data we decided not to do this.

However, let us summarize as far as we have gone. It would look as though in this type of activity we have a measure of goal-directed behavior. It appears only when the animal is moving towards the goal. If the animal is moving randomly in the box, just licking or cleaning it-