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### Interrelations Between Orbital Gyrus, Insula, Temporal Tip, and Anterior Cingulate

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In 1888 Sanger Brown and Schäfer reported that after complete bilateral temporal lobectomy monkeys showed marked tameness and inability to utilize sensory impressions, although primary sensibility seemed undisturbed. Klüver and Bucy in 1938 called attention to these findings in their report on bilateral temporal lobectomized monkeys. Besides the dramatic tameness which invariably followed the second ablation, these investigators reported that their animals would repetitively investigate objects by placing them in the mouth, would no longer distinguish between food and non-food objects, and would eat food previously rejected. They referred to this behavior as 'psychic blindness'. Ades and Raab have shown that visual discriminatory ability is lost following bilateral temporal ablations provided these are combined with bilateral lesions of the prestriate region (which, when removed by itself, does not permanently affect such a discrimination). More extensive studies by Chow, Blum, and Pribram show, however, that although the ability to learn to perform visual discriminations is markedly impaired by ablations of the lateral cortex of the preoccipito-temporoparietal complex, the animals' reaction to the visual stimuli discriminated is essentially unimpaired. Thus, the more medially placed structures of the temporal lobe were indirectly implicated in the gross behavioral changes noted above.

#### Anatomical and Physiological Studies

Von Bonin and Bailey suggested, on the basis of neuronographic and cytoarchitectural evidence, that the cortex of the temporal pole is functionally related to that of the anterior insula and orbital gyri. Although blood pressure and respiratory effects may be evoked from many cortical areas, a particularly marked effect may be evoked by stimulation of a continuous band of cortex extending from the anterior cingulate gyrus across the posterior orbital surface to the temporal tip. This observation was made by Kaada, Pribram, and Epstein in an extension of the studies on the function of the posterior orbital surface by Bailey and Sweet and Livingston *et al.* It suggested a possibly useful revival of the concept of a rhinencephalon. Pribram, Lennox, and Dunsmore have elucidated the neuronographic interrelationships of this region. In contrast to the lateral surface, only short projection systems were found linking the areas of the rhinencephalon. The close relationship of the orbitotemporal cortex to that of the cingulate and hippocampal formations was confirmed and clarified.

The relation of the rhinencephalon, as already defined, to the hypothalamus has been reviewed by Ingram. He concludes that there is reasonably good evidence for, among others, afferent connections to the hypothalamus from the rhinencephalon via the medial forebrain bundle, the fornix and the stria terminalis. The strychninization studies of Ward and McCulloch have added to this evidence as has the recent finding of Wall who has shown that the posterior orbital surface sends a fine fiber projection to the ventromedian nucleus of the hypothalamus and the head of the caudate nucleus. Wall has further shown that fibers affecting blood pressure project directly onto the hypothalamus from the orbital surface, while those affecting respiration do not. If a lesion is placed in the region of the ventromedian nuclei of the hypothalamus, stimulation of the orbital surface no longer evokes blood pressure changes while the respiratory effects may still be evoked. The respiratory pathway may pass via the caudate nucleus.

The relation of the deep projection systems from the orbital surface to those from the cingulate and temporal tip is not yet known but it contrasts with those from the lateral surface which affect the cardiovascular system. Pathways affecting blood pressure from the lateral surface do not appear to pass through the hypothalamus and may pass through the pyramidal tract.

## Psychophysiological Studies

To return to the behavioral aspects of the problem. Preliminary results of Peibram, Epstein, and Bar-Jay indicate that bilateral ablation of the posterior orbital surface of the frontal lobe, the anterior insula, temporal pole, and orbito-temporal cortex (with varying amounts of the amygdala) in the rat will give rise to the compulsive oral investigation of food and non-food objects previously noted after bilateral temporal lobectomy. These animals show this altered reaction not only to visual stimuli but also to somesthetic ones — even to pain. This is demonstrated when they repeatedly grasp and put in their mouths lighted matches and burning pieces of paper or sharp objects such as pieces of metal or nails. The animals react to the painful stimuli by reflex withdrawal or rubbing of the injured part — but immediately return to grasp and orally investigate another such injurious object. This altered response extends to taste: in the quinine water choice experiment devised by Patton and Ruch, these animals fail to avoid the quinine even in maximal concentrations. (It is significant that temporal lobectomized animals do not show this deficit in this situation, suggesting that at least part of the cortex subserving taste is located in the other portions of the orbito-temporal complex removed.) In spite of this, the animals continue to perform the visual discriminations (pattern, color) to which they had been trained preoperatively, suggesting that discriminatory disability is not necessarily involved in this altered behavior.

It is interesting that while these monkeys with orbito-temporal ablations show such compulsive oral investigation and altered reaction to stimuli, a monkey with hypothalamic hyperphagia shows neither of these abnormalities. On the other hand, since alterations in activity, food intake, and other metabolic processes are common to animals with either the cortical or hypothalamic lesions, an intensive analysis of these factors is now under way.

Among the many effects that have been observed following interference with the hypothalamus, those following bilateral electrolytic ablation of the region of the ventromedian nuclei, particularly on their lateral aspect, have recently been further elucidated. These are the lesions which the studies of Hetherington and Ranson, Brobeck, Tepperman and Long, Brooks and Lambert and Wheatley have demonstrated to lead to hyperphagia and obesity, changes in emotional behavior, some decrease in activity, gonadal atrophy and various — probably secondary — changes in carbohydrate and fat metabolism and in endocrine function. Although the rat has been the chief species used in these investigations, more or less similar observations have been made in the cat, dog, and monkey. The situation of these lesions is such that they may well interfere with all three of the rhinencephalo-hypothalamic connections mentioned above or with their target hypothalamic centers.

More recently Stevenson has reported that these lesions in the rat result in a marked upset in the animal's aqueous economy. Water loads administered by mouth are not delivered in the usual time or manner, two or three times the normal period being required for the animal to bring its weight back to the starting level and the proportion excreted as urine being abnormally small. That this phenomenon reflects a chronic embarrassment is demonstrated by the constant low water intake in relation to the amount of food consumed (water/food intake ratio) that such animals show. In this experimental condition there is also, apparently, an overactivity of the antidiuretic activity of the neurohypophysis: for measurements of renal glomerular filtration by creatinine clearances reveal a markedly greater tubular re-absorption of water in such animals than in normal controls.

These studies have been further extended in the rat by Stevenson, Welt, and Orloff. They have found that in these animals in the fed and watered state or in the fasted and thirsted state there is a significantly higher serum sodium level than in similarly treated controls. In the fasted but watered state it appears that although the response of the lesioned animals is not normal, there is a tendency to approach the level of serum sodium of the controls. These findings might be attributed to the high food and therefore high salt intake. However, Gamble, Putnam, and McKhann have shown that the normal response to an increase in salt intake is an increase in water intake. Confirming this under conditions similar to those of the hypothalamic studies, Stevenson and Zeppa recently have found that in normal animals an increased salt intake results not only in an increased water intake

but an increased water-food intake ratio, this is the opposite of the reaction in the hypothalamic animals studied. It is felt that these various studies provide some insight into possible mechanisms by which the thymopituitary may influence behaviour.

### Discussion

*Case II, Pyramus.* The first half of the film that you saw showed the animal preoccupied and the second half of the film was the operative behaviour. In an operational level, the behavioural changes we saw here can be described most easily in the test situation. The animals will repeatedly investigate all food objects and non-food objects in any situation in the home cage or when presented with these objects in a test situation.

They have been made or now being to discriminate between colored water and plain water. However, on the new discrimination test we have four such as color discriminations and visual pattern discriminations, these animals are able, in spite of this deficit in behavior, to perform visual discrimination tests. We, therefore, must speculate on the interpretation of this reaction. The speculation depends almost entirely on the particular type of stimulation which you use. We could say in physiological terms that these animals have an altered perception in these stimuli and an altered reaction on the basis of this perception.

In psychodynamic terms, on the other hand, we might say that these animals have regressed to a lower level of behavior. These, however, are speculations and we are hoping by various other tests in similar situations to come to a more operational definition of behavior deficits which these animals show.

*Food II, Aletia.* I was just going to ask Dr. Fillion and Dr. Pyramus without existing now about the general behavior of these animals, is we should not put on record that pythons who have no operative procedures will eat lighted cigars and cigarettes; it is a usual thing.

*John F. Fillion.* The fire-eating behavior was definitely a postoperative effect in the two pythons which Dr. Pyramus had under training. The behavioral change was also seen in monkeys, but the fire-eating effect has been seen only in the two pythons.