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Plasma Corticosteroids: Changes in Concentration after Stimulation of Hippocampus and Amygdala

Abstract. *Plasma 17-OH corticosteroid levels were determined before stimulation and at various intervals after stimulation in these limbic sites in patients in whom implanted electrodes had been placed during evaluation for surgical treatment of psychomotor epilepsy. Stimulation of the amygdala was followed by an elevation of plasma 17-hydroxycorticosteroids. Hippocampal stimulation resulted in a decreased corticosteroid level, followed in two instances by a secondary elevation.*

Selected patients under consideration for surgical treatment of uncontrollable, severe psychomotor seizures are being studied with depth electrodes at this medical center (*1*). Rigidly supported bipolar electrodes, electrically insulated except at the tips, are stereotaxically implanted in deep temporal lobe sites by the use of radiologically defined landmarks within the skull (*2*). They are maintained in position for 3 to 4 weeks, during which time extensive evaluation procedures, including electrical stimulation in the depth sites, are conducted. The necessity for stimulation during the clinical evaluation of these patients presented the opportunity to examine in man the possible influence of these limbic structures on the pituitary-adrenal system. Observations on laboratory animals, including primates, have indicated in general that stimulation of the amygdaloid nucleus activates the stress mechanism, whereas hippocampal stimulation inhibits it (*3*, *4*).

Observations were made on four patients, 2 to 3 weeks after electrode implantation. Blood samples (10 ml) were withdrawn from a peripheral (antecubital) vein in two patients and from a catheter threaded more centrally into the subclavian vein in two others. A 60-minute interval between catheter placement and collection of the control sample was allowed to elapse, during which the patient reclined quietly in bed. After the collection of several control samples, brain stimulation was carried out. Blood was collected at intervals after a 30-second train of unidirectional square wave pulses (5 volts, 10 per second, 1 msec duration). Samples were analyzed for plasma 17-OH corticosteroid level by the method of Peterson *et al.* (*5*) (phenylhydrazine reagent was increased from 0.2 to 0.4 ml per tube). Standard deviation for the method is ±8 percent for most of the range of values. Stimulation at these parameters in the subjects studied failed to evoke detectable subjective or behavioral alterations. Brief evoked responses but no after-discharge or persistent paroxysmal activity appeared in the electrical recordings from other depth sites.

Stimulation of the amygdala (see Table 1) was followed in every instance by an increase of 17-OH corticosteroids in the blood. This is consistent with a facilitation of the pituitary-adrenal stress mechanism. This finding is consistent with the observations in laboratory animals for stimulation of the baso-medial portion of the amygdaloid nucleus (*3*). Evaluation of the significance of these observations for a functional dichotomy between baso-lateral and baso-medial amygdala suggested by studies with animals (*3*) must await histological analysis of the electrode placement in the human subjects. The immediacy of this effect argues against the possibility of a decrease in the rate of corticoid removal by the liver being responsible for the change.

Stimulation of the hippocampus resulted in a moderate initial decrease in steroid level in all subjects. In one patient (No. 4) this decrease was followed approximately 30 minutes later by an increase above control levels, which suggests that a compensatory mechanism had been activated.

These observations with human subjects support the view that the structures of the limbic system of the brain are closely related to the pituitary-adrenal stress response mechanism (*6*). The precise anatomical implications of the study await histologic analysis of the removed temporal lobe specimens.

Table 1. Corticoid response to limbic stimulation.

Location of stimulation (x-ray approximate)	17-OH corticosteroid level (μg %)					Change (%)
	Control	Minutes after stimulus train				
		0 to 5	5 to 15	15 to 30	30 to 60	
	Patient No. 1 (blood from peripheral vein)					
Pes hippocampi	31.4				21.7	−28
	Patient No. 2 (blood from peripheral vein)					
Amygdala	20.9				23.5	+12
	Patient No. 3 (central veinous blood)					
R–Pes hippocampi	16.2	3.9	2.7	1.9	12.7	−88
L–Pes hippocampi	12.7		1.3	4.6	9.2	−90
R–Amygdala	9.2		33.6	32.4	17.4	+360
L–Amygdala	17.4		40.5		23.2	+232
	Patient No. 4 (central veinous blood)					
L–Amygdala	4.0	9.5	11.5	16.8	4.5	+415
L–Ant. hippocampus	7.3	6.0	6.0	7.1	16.1	−18 +230
L–Pes hippocampi	1.0	3.4	0.0	0.0	16.7	−100 +1600

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