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# MORPHOMETRY OF THE HUMAN PINEAL GLAND: RELATIONSHIP TO THE ADRENAL CORTEX

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**To investigate the role of the pineal gland in the endocrine system, we examined 26 autopsy cases dying from non-neoplastic diseases. The study was carried out on the hypothetic basis of the possible influences of the pineal gland on the pituitary-adrenal axis, which we believe to be existing also in man. Measurements on the pineal gland revealed that the weight of the gland was directly proportional to the volume ($r=0.94$; $P<0.001$) and also to the nuclear density of the parenchyme ($r=0.65$; $P<0.01$). Then, the interrelationship between the weight of the pineal gland and the thickness of the adrenal cortex was determined ($r=-0.56$; $P<0.05$). The pineal gland was significantly larger in weight in the prednisolone treated patients (166±66 mg, [±SD]) than in the others (97±52 mg; $P<0.05$). We conclude that the functional antagonism exists between the pineal gland and the adrenal cortex in man, although the mechanism involved has not been clarified yet. ACTA PATHOL. JPN. 30: 407~410, 1980.**

## *Introduction*

By modern approaches to pineal physiology, it has been proved that the pineal gland is involved in gonadal function, in photoreception and in changes of the skin color.

Moreover, several animal experiments have suggested that the pineal exerts an inhibitory influence on the adrenal cortex in rodents. But, as no sufficient data have accumulated about this relationship in man, we cannot guess the role of human pineal in the homeostatic mechanisms.

In this paper, to estimate this correlation in man, morphometry was carried out on the pineal gland and the adrenal cortex of the patients who died from non-neoplastic diseases.

## *Materials and Methods*

### *1. Materials*

A total of 26 human adult autopsy cases were studied. They consisted of 16 males and 10 females accumulated in our department over a period of recent 2 years. The age of the patients ranged from 16 to 85 years, the average being 54 years. In the present series, there were 7 cases with clinical history of glucocorticoid (prednisolone) treatment; 4 of systemic lupus erythematodes, one each of rheumatoid arthritis, progressive systemic sclerosis and interstitial fibrosis of the lung.

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*2. Methods*

At autopsy, the brain and the adrenals were fixed immediately in 10% formalin solution. About 4 weeks later, in each case, the pineal gland was resected from the brain, and the soft tissue covering the gland was removed as much as possible. After leaving it on a filter paper for a while, the weight of the pineal gland was measured by a direct reading balance (Shimazu L type, sensitivity 1 mg) as well as the length, the width and the thickness were by a slide caliper (sensitivity 0.1 mm). Then the volume of the gland was estimated by calculation, considering it as a spheroid body.

Paraffin-embedded sections of the pineal gland and the the adrenal gland, cut in 4 $\mu$m thickness, were stained with hematoxylin and eosin. The following stains were also used; Azan-Mallory's and modified Rio-Hortega's for the pineal and Azan-Mallory's and Watanabe's silver impregnation for the adrenals.

Morphometry of the pineal gland was carried out with 19 cases. The nuclear density was determined at 15 different fields of the parenchymal lobules in each gland by point counting method, using 121 points in a squarelattice eyepiece at $\times$ 400 magnification. Arithmetical mean and sample standard deviation were calculated by regarding a sequence of 3 fields as one sample.[10]

Measurement of the thickness of the adrenal cortex was carried out on 24 pairs of adrenals. The thickness of the cortex was determined microscopically with a micrometer at a magnification of $\times$100. After 20 random trials with the bilateral cortices of each case, the result was analysed by arithmetical mean and sample standard deviation.

## *Results*

*1. Measurements of the Pineal Gland*

The volume was estimated in 21 cases. Figure 1 shows the evidence that the weight is directly proportional to the volume ($r=0.94$, $P<0.001$). This result indicates that (a) the process of fixation has probably no undue effect on these gland and (b) the density of the glands is uniform in the fixed condition, i.e. about 1 mg per $mm^3$.

Figure 2 shows the interrelationship between the weight and the transectional nuclear density of the pineal gland ($r=0.65$, $P<0.01$). This result suggests that increases in the pineal weight reflect the densely packed parenchyme.

*2. Interrelationship between the Pineal Gland and the Adrenal Cortex*

The relation between the weight of the pineal gland and the thickness of the adrenal cortex is shown in Figure 3. A progressive decrease of the pineal weight was seen as the thickness of the adrenal cortex increased ($r=-0.56$, $P<0.05$). Pineal gland weights were significantly higher in the glucocorticoid-treated patients ($166\pm66$ mg, [$\pm$SD]) than in the other patients ($97\pm52$ mg, $P<0.05$ by Student's t-test).

## *Discussion*

More than several animal experiments have been performed to suggest that the pineal gland exerts an inhibitory effect on the pituitary-adrenal axis. However, no such evidence has been known to us within the scope of human physiology or pathology.

In the present study, we have observed the inverse interrelationship between the weight of the pineal gland and the thickness of the adrenal cortex. This result probably suggests that the functional antagonism exists between these two organs, although the mechanism involved is uncertain.

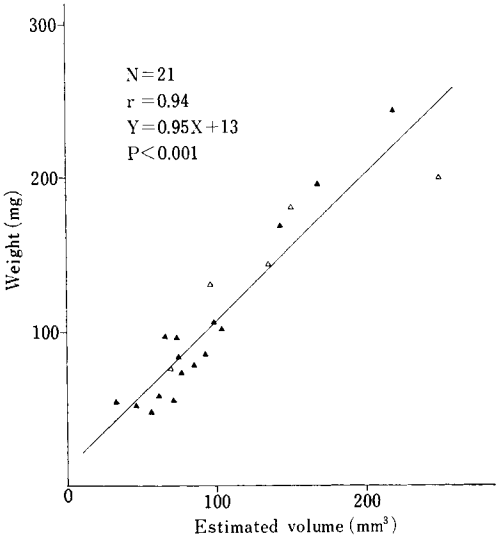



Fig. 1.

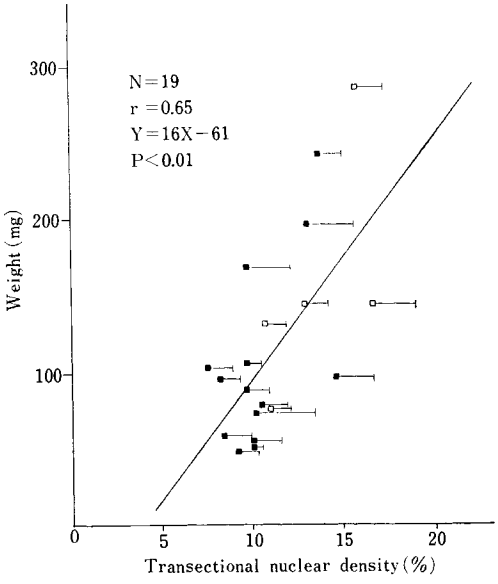
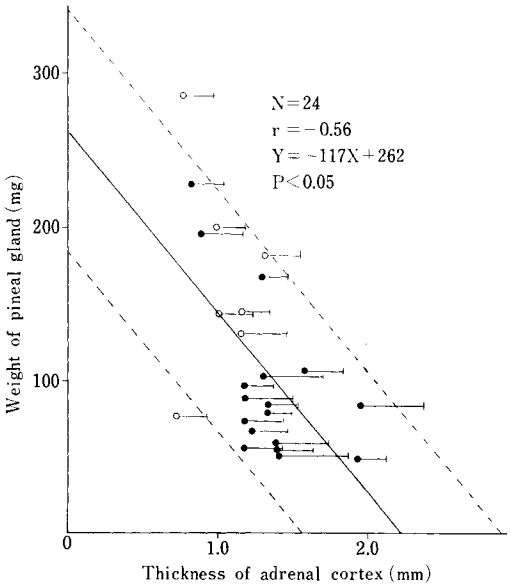



Fig. 2.

Fig. 1. Correlation between the volume and the weight of the pineal gland in 21 of the 26 patients (r=0.94, P<0.001). △; cases with positive history of prednisolone treatment. ▲; others.

Fig. 2. Correlation between the nuclear density (mean+SD) and the weight of the pineal gland in 19 of the 26 patients (r=0.65, P<0.01). □; positive history of prednisolone treatment. ■; others.

Fig. 3. Correlation between the thickness of the adrenal cortex (mean+SD) and the weight of the pineal gland in 24 of the 26 patients (r=−0.56, P<0.05). The dotted line represents the normal range (95% confidence limits). ○; positive history of prednisolone treatment. ●; others.




Before the 'melatonin era', VON KUP (1937) described his hypothesis in the autopsy report of a 3.5-year-old boy that there seemed to be an indirect functional antagonism between the pineal gland and the adrenal cortex.[6] ARIETI (1954) introduced

his idea that the pineal gland is involved in some kind of non-specific defence mechanism as the adrenal cortex and the pituitary are[1].

In the animal experiments, several workers showed that pinealectomy caused adrenal hypertrophy compared to sham operated controls in rats (IZAWA, 1926; WURTMAN *et al.*, 1959; HOUSSAY *et al.*, 1968; FRASCHINI *et al.*, 1968) and in mice (VAUGHAN *et al.*, 1972) and that the administration of melatonin or bovine pineal extract to either controls or pinealectomized animals resulted in decrease in adrenal weight (WURTMAN *et al.*, FRASCHINI *et al.* and VAUGHAN *et al.*).

On the contrary, there are negative reports of a few authors who failed to find the functional relationship between these organs (DE PROSPO *et al.*, 1971; BARCHAS *et al.*, 1969).

At present, we cannot evaluate the significance of the result that the weight of the pineal gland was heavier in the patients who had been treated with prednisolone than in the others. Estrogens and other sex steroids have been shown to have the property to modulate the pineal melatonin synthesis[7]. Glucocorticoids may also play a part in the regulation of pineal function directly or indirectly, but no sufficient data are available concerning this point now.

Measurement of melatonin in human plasma, which has become possible only recently, may establish the role of the pineal in the general adaptation syndrome (SELYE).

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