THE SIGNIFICANCE OF HORMONAL DISTURBANCES FOR THE DEVELOPMENT OF MENTAL DISEASES’
(A REVIEW)

BY

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The subject of my address is so comprehensive that I cannot give a proper survey of the conditions within the limited time at my disposal. I shall therefore confine myself to mention some of the most important features and concentrate especially on features in which I myself have taken particular interest.

The neuro-hormonal correlation is very complex, there being a close relationship between the psychic functions, the function of the pituitary-hypothalamic system, and those of the subordinate endocrine glands. These different functions influence each other, so that the least disturbance of one of them will almost inevitable lead to a vicious circle.

It is a well-known fact that purely psychic functions, e.g. emotion, may give rise to endocrine disturbances. Best known is the occurrence of amenorrhea or other menstrual disturbances with various psychic insults and mental diseases. Furthermore, recovery from a psychosis or other mental affection is often seen to be attended by a return to normal hormonal conditions.

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It is, therefore, no wonder that many endocrine lesions are associated with pronounced mental symptoms. The physiopathological conditions are not yet quite clear, but presumably there occurs first a disturbance of the general metabolic processes of the brain, which is then followed by development of a physiopathological activity. Possibly the brain acts as a reservoir for certain hormones (Reiss, 1944).

The endocrine diseases causing mental symptoms are chiefly those occurring in pituitary(-hypothalamus), gonads, and thyroid.

With regard to the pituitary lesions there is reason to remark that the pituitary body is so intimately connected with the hypothalamus, both neuro-anatomically and physiologically that they constitute a functional entity. The hypothalamus is, however, supposed to possess an independent secretory activity as well.

Mental symptoms are not a common occurrence in conditions due to hyperfunction of the pituitary body (hyperpituitarism). In conditions due to pituitary hypofunction (hypopituitarism), on the other hand, such symptoms are frequent, particularly so in adiposo-genital dystrophy. This condition being probably due chiefly to a lesion in the hypothalamus, it is reasonable to presume that it is the hypothalamus which is responsible for the mental symptoms in association with pituitary lesions.

The mental symptoms seen in association with hypopituitarism may, according to the literature be either torpidity and indolence, or irritability and emotional instability.

Personally, on examination of a number of patients with pituitary-hypothalamic lesions (Leth Pedersen, 1948), I believe to have ascertained characteristic mental symptoms in the forms of: 1) increased irritability, these patients being emotionally unstable and hot-tempered to the point of explosion, and therefore frequently at variance with their associates; 2) emotional instability, the patients being sensitive with fluctuating moods and a tendency to low spirits; 3) ego-
centricity, the patients being self-pitying, preoccupied about themselves and their disease, inert and despairing, sluggish, self-willed, and hard to please. In my material these symptoms were observed partly in patients with different forms of hypopituitarism, and partly in young women with a characteristic clinical picture, presumably caused by a hypothalamic insufficiency. This picture corresponds exactly to that described by Bartels & Hjorth (1947) and designated by them as hypogonadism. The disease occurs exclusively in women within the former half of the sexually mature age, and it manifests itself by gain in weight and the development of a characteristic «healthy, flourishing» appearance. The basal metabolic rate is low, the menses scanty, the libido decreases, and the patients develop the mental symptoms just mentioned, generally attended by tiredness, headache, and different vasomotor disturbances.

Lesions of the gonads are far more frequent among women than among men. I shall here concentrate on the conditions in women.

It is a well-known fact that mental symptoms are of frequent occurrence at the menopause, when a gradual involution of the ovaries takes place. There seems to be no doubt that these mental symptoms, characterized particularly by emotional instability and increased irritability, are released by the ovarian insufficiency, but we are not quite clear as to the physiopathological conditions.

Emotional disturbances are seen also during menses, in the form of dysphoria or the like, the cause of which is not evident either. The possibility has been suggested of a connection with disturbance of the water metabolism due to an increased production of steroids (Hemphill, 1944). Similar mental disturbances may be met with during pregnancy and puerperium.

»Menopausal« symptoms are more pronounced in women after castration, whether by X-rays or operation. I have personally (Leth Pedersen, 1944) examined over 50 women (observation periods up to 20 years) after removal of both ovaries
at the sexually mature age (from the menarche till the age of 40). All these women had hot flushes and also mental symptoms of some kind or other.

The mental symptoms occurring were as follows: 1) disquiet and restlessness. 2) increased irritability with emotional instability and irascibility. These 2 groups of symptoms were present in well over half of the examined women. 3) change of mood in the direction of instability and a tendency to low spirits, likewise found in well over half of the women. 4) impaired memory and failing power of concentration, occurring in ab. 50 per cent. 5) fits of palpitation, dyspnoea, and anxiety, likewise ascertained in ab. 50 per cent. In consequence of these symptoms the ability to work was more or less reduced in a scant 50 per cent of the examined women. The mental symptoms were found to be most conspicuous in the patients with the most pronounced hot flushes, a symptom which, in my opinion, may to a certain extent be taken as a measure for the degree of ovarian insufficiency. I, therefore, believe the ovarian insufficiency to be the cause also of the mental symptoms. This view is supported by the fact that the mental symptoms improve in all cases after large doses of oestrogen and are likely to disappear entirely if only oestrogen is administered in sufficient doses.

Nearly all the female castrates whom I have examined made an energetic and diligent impression, and rather minimized their symptoms, being by no means egocentric, inert, self-pitying, despairing, or preoccupied about themselves and their disease. They differ by this feature and by their restlessness from the women with hypothalamic insufficiency. In my opinion the two different conditions of hormonal insufficiency are attended by distinct and characteristic mental pictures.

Mental symptoms are conspicuous also in association with thyroid lesions, presumably because of the effect of these lesions on the hypothalamus. Thus, in the case of hyperthyroidism there are found signs of sympatheticotonia with emotional instability and increased irritability (Reiss, 1944),
whereas hypothyroidism is attended with a reduced sympathetic tone with slow reactions and little affectivity.

Adrenal lesions are not attended by constant or characteristic mental symptoms. But attention has for many years been focussed on the adrenals as the possible centre for the pathogenesis of schizophrenia and certain neuroses, especially neurasthenia, probably because these cases somatically resemble the cases with adrenal insufficiency.

It is a fact that there is found a greater proportion of mental cases among dyscrinous patients (notably among those with lesions of pituitary body and ovaries) than among patients without endocrine diseases. Hence there must be a certain relationship between dyscrinism and mental diseases, particularly schizophrenia. However, no psychosis has so far been established to have a purely endocrine aetiology (Hemphill, 1944).

As regards schizophrenia, nothing certain is known as yet of the pathogenetic importance of the adrenals. The facts that schizophrenic women are far more often affected with hypertrichosis than normal women (Smith, i. 1944, Lohse & Bjarnhjedinson, 1945), and that the adrenal cortex is of importance for hypertrichosis in women, have prompted me to study the 17-ketosteroid excretion in 64 women, comprising both schizophrenics and mentally normal (Leth Pedersen, 1947). Within both groups those with hypertrichosis as well as those with normal hairiness were examined. I thereby found a tendency to increased 17-ketosteroid excretion (and therefore probably to increased 17-ketosteroid production) in the hypertrichotic women, but independent of whether they suffered from schizophrenia or were mentally normal. Furthermore, there was found no increase in the 17-ketosteroid excretion in schizophrenic women with normal hairiness. Thus, the 17-ketosteroid production as such is hardly likely to play any part in the pathogenesis of schizophrenia. This does not preclude, however, that other functions of the adrenal cortex may be of pathogenetic importance.
Formerly lesions of the female sexual glands were supposed to be associated with specific psychosis. Menopausal psychoses, for instance, have been described, in particular the »involution melancholia« and paranoid mental diseases. However, it seems now to have been proved that specific menopausal psychoses do not exist. At the menopause there is found an increased psychic vulnerability and consequently increased morbidity with regard to the commonly known psychoses; and the menopause may to some extent mark these psychoses, particularly in the forms of anxiety or sexual colouring (Dickmeiss, 1940). The same is the case with regard to female castrates. Here, too, troubling mental symptoms are, as already mentioned, of frequent occurrence, but there is found no specific castration psychosis. Similar conditions assert themselves during the puerperium. Thus, there are hardly found specific puerperal or lactational psychoses, but during these periods there is increased morbidity with regard to the commonly known psychoses, presumably due to hormonal disturbances, possibly in connection with toxic influences.

It has been demonstrated both clinically and experimentally that the hypothalamus is of particular importance for the emotional life. Hence the investigations made within recent years into the aetiology and pathogenesis of the manic depressive psychoses have been concentrated particularly on the hypothalamus. However, we have not yet been able to prove that the manic depressive psychosis is released from a lesion or a dysfunction of the hypothalamus. An interesting observation is that of a relationship between thyroid lesions and manic depressive psychosis, which is suggestive of a common (probably hypothalamic) cause of the two diseases (Ostenfeld, 1944 and 1947).

Another point of importance for the study of the hypothalamus and its significance within psychiatry is that of the pathogenesis of hysteria. I have mentioned that in patients with pituitary-hypothalamic insufficiency I have found mental changes manifesting themselves particularly as increased irritability, emotional instability, and egocentricity, symptoms
which, when occurring jointly make these patients seem »hysterical«. I have observed similar mental symptoms, but coming on in fits, in other patients, who had psychomotor attacks as well (Leth Pedersen, 1948). These attacks were diagnosed as hysterical in neuropsychiatric departments; but encephalography revealed here cerebral atrophy of the ventricular type. In all these cases I find it reasonable to presume that the mental symptoms were due to lesion of the vegetative (or hormonal?) centres of the hypothalamus.

It is a well-known fact that hysterical symptoms may occur after organic cerebral lesions (among others encephalitis and cranial traumas). Moreover, it does not seem unlikely that the function of the vegetative centres in the diencephalon may be damaged with development of hysterical symptoms or other neuroses, as suggested among others by von Monakow in his so-called plexus-theory. Von Monakow states here that the bloodliquor barrier may fail because of functional influences, such as strong emotions and the like, by which the central nervous system is exposed to toxic influences, against which it is commonly protected. Even though the release of the hysterical reaction is mentally conditioned, there can hardly be any doubt that there is an underlying somatic predisposition, presumably a hypersensitiveness of the hypothalamic centres (Brun, 1946). This somatic predisposition is probably acquired in the majority of the cases.

**SUMMARY**

A brief survey is given of the occurrence of mental symptoms in association with endocrine lesions. The possibility is suggested of an endocrine aetiology of certain mental diseases, notably those with emotional instability and hysterical symptoms.

The author gives an account of own studies concerning patients with lesions in or about the hypothalamus and women castrated by operation. Rather characteristic mental symptoms have been found in both groups of patients, particularly with-
in the field of emotion, with symptoms of emotional instability and increased irritability, but not identical in the two groups. Thus the patients with hypothalamic lesion are characterized besides by a marked egocentricity, they being self-centred and hard to please, inert and despairing, whereas the female castrates by no means are self-centred, despairing or inert, but restless and rather minimizing their symptoms.

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