

Psychological aspects of endocrine disease*

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ABSTRACT This review illustrates how an innovative psychoneuroendocrine approach to endocrine patients may improve their management. Important psychological issues pertain to all the different phases of an endocrine disorder. Before disease onset, stressful life events may play a pathogenetic role and, together with chronic stress, may contribute to a cumulative burden also called allostatic load; psychological and psychiatric symptoms are common both in the prodromal and in the active phase of illness; after cure or remission, there could be residual symptoms and impaired quality of life that deserve attention. All these aspects should be taken into consideration and introduced in current endocrine care and practice.

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INTRODUCTION

In recent years, a number of studies have documented important morbidity and impaired quality of life in patients with various forms of endocrine disease.¹ Psychological distress was often found to persist even with cured, or acceptably compensated, endocrine disorders of different kinds.^{1,2} As the issues of psychological wellbeing, functional capacity, and social and interpersonal components of medical illness develop further,³ the area of quality of life may also provide new insights in clinical endocrinology. Research evidence for an updated psychosocial comprehension of endocrine disease is available. This paper will focus on areas in endocrinology where attention to the psychological aspects of illness may have significant clinical and research implications.

THE CONSEQUENCES OF STRESS

In 1993 McEwen and Stellar⁴ proposed a formulation of the relationship between stress and the processes leading to disease based on the concept of allostasis, the ability of the organism to achieve stability through change. The concept of allostasis emphasises that healthy functioning requires continual adjustments of the internal physiological milieu. In response to environmental demands, different physiological systems interact with different levels of activity. Allostatic load refers to the wear and tear which results from either too much stress or inefficient management of allostasis. The definition of allostatic load reflects the cumulative effects of

experiences in daily life that involve ordinary events as well as major challenges.⁵ Subtle and longstanding life situations should not be readily dismissed as minor or negligible, since chronic, daily life stresses may be experienced by the individual as taxing or exceeding his/her coping skills with consequences that are of both a psychological and physical nature.^{6–8} These aspects are often overlooked in conventional thinking about ‘stress’.

In addition to chronic stress, life events may play a considerable role in uncovering a person’s vulnerability to a particular physical or psychiatric disorder.^{9,10} ‘Life events’ are isolated changes in the person’s social or personal environment, that should be external and verifiable rather than internal or psychological. Using structured methods of data collection and control groups, recent life events, that is events in the year before disease onset, have been demonstrated as playing an aetiological role in some endocrine disorders.¹

Several interesting issues have arisen during the study of Cushing’s syndrome. Stressful life events in the year prior to first signs of onset were explored by Paykel’s Interview for Recent Life Events¹⁰ in an equal number of patients with Cushing’s syndrome and healthy subjects matched for sociodemographic variables.¹¹ Patients with Cushing’s syndrome reported considerably more unwelcome and uncontrolled events than controls. When patients with pituitary-dependent Cushing’s disease and patients with pituitary-independent Cushing’s

syndrome were assessed separately and compared with their matched controls, a causal role for stressful life events was found exclusively in Cushing's disease;¹¹ supporting the theory of a limbic-hypothalamic involvement in the pathogenesis of this condition.¹² Using the same method, life events were explored in 70 patients with Graves' disease and found to be much more frequent in patients than in controls.¹³ The same conclusions were drawn by other studies.¹⁴⁻¹⁶ Life events have also been investigated in patients with hyperprolactinaemia, where they were significantly more frequent than in controls.¹⁷

In clinical endocrinology, exploration of psychosocial antecedents may explain:

- temporal relationships between life events and symptom onset or relapse;
- presence of grief reactions, including the loss of a body part or bodily function. Gradual changes which occur with chronic progressive disease may give the individual time to perceive and tolerate the changes, whereas sudden modifications are potentially more disruptive and grief-inducing;¹⁻³
- perception of an environment by the person as exceeding his/her resources (allostatic load). Often patients deny a relationship between their allostatic load and symptomatology, since they are unaware of the latency between stress accumulation and symptom onset. This may be important in assessing patients with borderline laboratory findings (e.g. slightly elevated prolactin levels). Appraisal of life stress may have implications for clinical decisions, such as termination of the long-term pharmacological treatment in hyperprolactinaemia, and in the presence of unexplained somatic symptoms or delayed recovery.¹⁻³

PSYCHOLOGICAL SYMPTOMS

Endocrine disorders may be associated with a wide range of psychological symptoms. At times, such symptoms reach the level of psychiatric illness, mainly mood and anxiety disorders.¹ Other times, however, psychiatric nosography fails to capture psychological distress and this can only be identified by the use of the subclinical forms of assessment, such as the Diagnostic Criteria for Psychosomatic Research (DCPR).³ This paper will briefly describe the main psychological correlates of endocrine disease, including both psychiatric (Table 1) and psychological (Table 2) syndromes. On occasion, psychological symptoms may precede other manifestations of an endocrine disorder and/or be early indicators of its relapse.¹⁸

Depression

Depressive symptoms are often encountered in the medically ill,^{1,3,18} but only some will suffer from a major

TABLE 1 Clinically significant psychiatric morbidity in endocrine disorders

Endocrine disorder	Psychiatric characteristics
Hyperthyroidism	Major depression, often associated with anxiety and irritability is the most common complication. It may be present in the prodromal phase. It is generally responsive to adequate endocrine treatment. Sometimes, antidepressant drugs are required.
Hypothyroidism	Depression, paranoid symptoms and cognitive disturbances may be present. Depression may occur in the prodromal phase.
Hyperparathyroidism	Depression and cognitive symptoms may occur. They may be present also in the prodromal phase.
Polycystic ovary syndrome	Depression and generalised anxiety symptoms may be present.
Hyperprolactinaemia	Depression, hostility and anxiety are common. Bromocriptine was found to be superior to placebo, while antidepressant drugs were ineffective.
Primary aldosteronism	It is particularly associated with anxiety disorders.
Cushing's syndrome	Major depression may affect about 50% of patients. It occurs in both pituitary-dependent and -independent forms, and may be present in the prodromal phase. Antidepressants are often ineffective, while inhibitors of steroid production are generally effective. Anxiety is frequently present. At times, mania may alternate with depression.
Addison's disease	Depression (characterised by apathy, social withdrawal and irritability) is often present and generally responsive to steroid replacement. It may occur in the prodromal phase.

depressive disorder. When depression is associated with a physical disorder, the potential relationships in the development of the mood disturbance range from a purely unexpected occurrence to a direct causal role of organic factors. The latter comes under the rubric of symptomatic depression or organic mood disorder, whose key feature is the resolution of psychiatric disturbances upon specific treatment of the organic disease.^{1,3,18} Symptoms of depression are frequently associated with endocrine disorders (Table 1), and particularly with Cushing's syndrome.^{1,12} Other endocrine disorders that may be associated with severe depression are hyperthyroidism, hypothyroidism,

TABLE 2 Clinically significant psychological clusters in endocrine disorders

Endocrine disorder	Psychological characteristics
Hyperthyroidism	Irritability is very common and is often associated with anxiety and depression
Hyperprolactinaemia	Hostility and irritable mood are frequently present together with persistent somatisation and demoralisation
Primary aldosteronism	Demoralisation is frequently reported in conjunction with anxiety.
Cushing's syndrome	Demoralisation and irritable mood are common both in the acute phase of illness and in the phase of recovery, particularly when the latter is delayed

hyperparathyroidism and hyperprolactinaemia^{1,18-22} and, to a lesser degree, polycystic ovary syndrome.²³⁻²⁵

Mania

This can be defined as a period of abnormally and persistently elevated and expansive mood (with symptoms such as decreased need to sleep, distractibility, increase in goal directed activity, excessive involvement in pleasurable activities and pressure to keep talking) and is far less common than depression in the medically ill.^{1,3,12,18}

Anxiety

This can be defined as a feared anticipation of an impending but intangible danger, and may be related to endocrine illness in a number of ways: it may occur as recurrent, prominent attacks or as generalised anxiety. As with depression, when anxiety disorders are associated with medical illness, potential relationships range from coincidental occurrences to a direct causal role of hormone imbalances. The relationship of anxiety to hyperthyroidism demonstrates this controversial aspect. Anxiety disorders may be precipitated by hyperthyroidism and may decrease with treatment, but may also predate its clinical manifestations or predispose to its onset.^{1,18} It is significant that anxiety symptoms in pheochromocytoma do not satisfy the psychiatric criteria for an anxiety disorder.²⁶ A noteworthy association between anxiety disorders (mainly generalised anxiety disorder) and primary aldosteronism has been reported recently.²⁷

Irritability

This has been associated with several endocrine disorders. A survey of neuropsychiatric complaints of 137 patients with Graves' disease²⁸ found that it was the most frequent symptom, occurring in nearly 80% of patients. In women with hyperprolactinaemia, hostility and irritable mood were consistently reported and were

receptive to lowering of plasma prolactin levels by bromocriptine but not to placebo.^{1,29} Irritability is often dismissed as a logical reaction to hospitalisation, pain and diagnostic procedures. However, it becomes a condition worthy of attention when it is characterised by a prolonged and generalised state, with difficulties in controlling temper, or by angry, volatile attacks that are unfamiliar to the patient. In a study comparing irritable mood in a variety of medical conditions,³⁰ it was significantly more prevalent in the settings of cardiology and endocrinology, compared to oncology and gastroenterology. Irritable mood was found to occur in 46% of 146 patients who had been successfully treated for endocrine disease.³¹

Demoralisation

This is a psychological syndrome characterised by the patient's consciousness of having failed to meet his or her own expectations or those of others or being unable to cope with some pressing problems.³² It involves distressing feelings ascribed at times by the patient more to failures and deficiencies in his/her environment (helplessness) and at times more to his/her own personal failures and inadequacies for which he/she feels nothing can be done (hopelessness). In the various phases of endocrine diseases (the frequently long interval from the appearance of the first symptoms to the establishment of a proper diagnosis, the period for endocrine work-up which may be lengthy and fatiguing, the length of time required to recover after surgery or radiotherapy), there are important sources of demoralisation. Demoralisation was found to occur in about one-third of remitted endocrine patients, with rates similar to those which were found after myocardial infarction or heart transplantation and in oncology.³³ Sometimes demoralisation may occur in conjunction with major depression, but in most cases it is independent.³³

Persistent somatisation

Somatisation is the tendency to experience and communicate psychological distress in the form of physical symptoms and to seek medical help for them. These functional symptoms may occur in conjunction with endocrine disturbances and may aggravate the clinical picture. In a sample of 146 patients with remitted endocrine disorders, persistent somatisation was found to occur in about 1 in 5 patients.³¹

RESIDUAL SYMPTOMS

Psychiatric disturbances and impaired quality of life, which were present in the acute phase of illness, are often found to improve upon normalisation of hormonal parameters.¹ However, in recent years there has been increasing awareness of the unsatisfactory degree of remission that current therapeutic strategies entail in a variety of endocrine disorders. Medical and psychiatric symptoms may persist as residual symptomatology and

amelioration of quality of life is not always the case. Indeed, in an investigation of 146 patients treated for endocrine disease (86 with pituitary and 60 with non-pituitary disease), 62% presented with at least one psychiatric diagnosis, whereas 66% suffered from at least one of the three DCPR syndromes considered (demoralisation, irritable mood, persistent somatisation).³¹ A total of 81% of patients presented with either a psychiatric or psychological (DCPR) diagnosis. About one-fifth of the patients had a DCPR cluster only.³¹ Against expectations, there were no significant differences between patients with pituitary and non-pituitary disease.

There may be different reasons for a delayed or impaired process of recovery. Hormonal alterations are frequently associated with affective disturbances, which do not always remit upon normalisation of blood parameters. When surgery is performed (e.g. pituitary microadenomectomy in Cushing's disease) the patient is likely to have expectations of a quick recovery toward his/her former normal condition. Unrealistic hopes of 'cure' may foster discouragement and apathy. Quality of life may often be seriously compromised when the patient is apparently doing fine (by a hormonal viewpoint). Hormone replacement may not fully restore optimal endocrine balance and subtle dysfunctions may still exert their influences on psychological states. Patients may display considerable impairment in self-esteem, body image distortion, disruption in interpersonal relationships, and social withdrawal. This has been observed in several studies concerned with patients with endocrine disease.^{1,2,12,34-37}

Research on quality of life has frequently emphasised the discrepancies in health perceptions between patients, their companions and their treating physicians.³⁸ In clinical endocrinology, there is often the tendency to rely exclusively on 'hard data', preferably expressed in the dimensional numbers of laboratory measurements, excluding 'soft information', such as disability and wellbeing. This soft information can now, however, be reliably assessed.³⁹ The evidence that has been gathered should lead endocrinologists to a multidimensional assessment of treatment effects, including psychosocial parameters.

CONCLUSIONS

The interrelationship between hormone abnormalities and psychological factors is complex and should be viewed in a multifactorial frame of reference. New challenges are emerging for patient management in clinical endocrinology and, as it happened in other fields

of clinical medicine, a conceptual shift from a merely biomedical approach to a broader consideration of the person and his/her quality of life appears to be necessary for improving therapeutic effectiveness.^{2,12} With this in mind, we introduced the concept of rehabilitation in endocrinology^{2,40} and tried to translate into operational terms the acquisitions of current psychosomatic research starting an innovative psychoneuroendocrinology outpatient clinic.⁴¹ Applying interdisciplinary expertise and addressing the need for rehabilitation in current endocrine practice is likely to improve final outcomes.

SUMMARY

Psychological aspects are important components of endocrine conditions that have only recently been systematically addressed in clinical research and practice. They pertain to all phases of illness. Recent stressful life events (within the year preceding disease onset) have been demonstrated to play an aetiological role in pituitary-dependent Cushing's disease, Graves' disease and hyperprolactinaemia. Both stressful life events and chronic stress contribute to a cumulative burden, also called allostatic load, which may uncover a person's vulnerability.

After endocrine abnormalities are established, they are frequently associated with a wide range of psychological symptoms. At times, such symptoms reach the level of psychiatric illness (mainly mood and anxiety disorders); other times they are subclinical (irritable mood, demoralisation, somatisation), but can be identified in clinical research by specific research tools. Longstanding endocrine disorders may imply a degree of irreversibility of the pathological process and induce highly individualised affective responses. In recent years, there has been growing interest in the presence of residual symptoms after adequate treatment.

In patients who show residual symptoms with persistence of psychological distress upon proper endocrine treatment, responding to their specific needs is likely to improve the level of remission. The support provided by an interdisciplinary approach, psychiatric or psychological interventions and rehabilitation measures may be of great value. As it happened in other fields of medicine, a conceptual shift from a merely biomedical care to a broader consideration of the person and his/her quality of life may be required for improving effectiveness in the management of endocrine patients.

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