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REVIEW

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The connection between depression and diabetes mellitus — current state of research

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Abstract

Chronic somatic disorders, including diabetes mellitus (DM), are often accompanied by mental disturbances, mainly of the anxious-depressive character. Their supposed etiology in this context are monoaminergic disturbances in CNS (central nervous system). The cause of depression in diabetics may be attributed to the stress related to the presence of a chronic disease, as well as to CNS damage in the course of DM. Psychosocial factors are also referred to as being the cause of depression in diabetic patients. According to some hypothesis, depression has an impact on hyperglycaemia and increases the risk of developing DM through unidentified mechanisms. Studies conducted so far did not yield unequivocal evidence for the etiology of both coexisting diseases and for the relation between depression and the pathologic factors accompaning diabetes mellitus.

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Somatic diseases, especially the chronic ones, are often accompanied by mental disorders, mainly of the anxious-depressive character.

This concerns diabetic patients, whose tendency to develop the above disturbances may be related to monoaminergic disorders in the central nervous system (CNS) [1–3]. The functioning of CNS neurotransmitters has been described based on an animal model, where the induction of DM in rats was followed by an increase in noradrenalin concentration in prosencephalon [4] and striatum and a decrease in adrenalin and noradrenalin concentration in hypothalamus [5, 6]. What is more, a decrease in serotonin metabolites has been observed [4, 6], probably due to a decrease in tryptophan content [7].

The increase of dopamine concentration in the brain of diabetic animals is accompanied by a decreased activity of dopaminergic neurons [5, 6], probably due to a suppressing influence of hyperglycaemia [8]. Moreover, a decreased concentration of D1 receptors [9] and an increased concentration of D2 receptors [10] were observed in striatum.

Autopsy examination of diabetic patients confirmed the differences in neurotransmitters content [4], but the investigated population was subject to other coexisting neuroendocrinological diseases, which could influence the results.

The symptoms of unstable diabetes mellitus, for example atypical and odd behavior in the state of hypoglycaemia, can form a similar picture to that of a psychotic disorder.

The cause of depression in diabetics may be attributed to the stress related to the presence of a chronic disease, as well as to CNS damage in the course of diabetes [1, 3]. Depression itself has a reciprocal destabilizing action on diabetes, impairing the patient's self control [3].

Lustman et al. [11] observed that more than 25% of diabetic patients fulfill the clinical criteria of depression, which is by far a larger percentage than that of the general population.

Thomas et al. [12] confirmed that type 2 diabetes mellitus is accompanied by an increased incidence of affective disorders. This is in contradiction with the result obtained by Weyerer [13], who did not find any differences between the patients with diabetes mellitus and those suffering from other somatic diseases. Thomas documented a twofold higher incidence of anxious-depressive states in women than in men, especially in those with a low socio-economic status.

The American investigators Ciechanowski et al. [14], in a study conducted on 367 patients with type 1 or 2 diabetes mellitus, found a relation between depression in diabetic patients and a non-compliance with dietetic recommendations.

Lustman et al. [11], in turn, analyzed several studies conducted on groups of 12–188 diabetic patients aged over 18 years and found a relation between depression in these patients and hyperglycaemia and a poor control of glycaemia. The role of this last factor is pointed out by Gary et al. [15] in an American study conducted on a group of 183 type 2 diabetic patients aged 35–75 years, as well as by the authors [16] of a Finnish population observation of 53 000 people aged under 65 years, where 260 type 2 diabetics were evaluated.

The studies investigating the coexistence of diabetes mellitus and depression emphasize the prevalence of diabetes complications [17, 18], impaired quality of life [16], increased health-related costs and expenses [19], poor body mass control [20] in the group of patients characterized by mood disorders or an overt depression.

Palinkas et al. [21], by examining 1586 Americans aged over 50 years, established that depression may be an answer to psychosocial stress caused by diabetes. The same conclusion was reached by Rajala et al. [22] after examining 1008 Finnish patients, pensioners or retired born in 1935.

The role of psychosocial factors in the etiology of depression in diabetic patients has been repeatedly investigated. A number of factors was identified, including female sex [19], a younger age [19, 23], single status [16, 19, 24], the kind of treatment prescribed (oral therapy) and a low income [18, 24, 25]. The significance of a lower economical status [18, 25] has been emphasized, among others, by Peyrot and Rubin [24] in an American study conducted on 634 patients and by Americans Karlson and Agardh [25], who examined 155 patients with insulin dependent diabetes aged 35.3 ± 8.9 years.

The impact of a poorer physical health on the manifestation of depression [19, 25] was noticed by, among others, de Groot et al. [26] in an American study analyzing 33 patients with type 1 diabetes and 39 patients with type 2 diabetes.

Miyaoka et al. [27] in a study conducted on a group of 151 Japanese with non-insulin-dependent diabetes established that a lack of social support is another etiologic factor of depression.

The lack of control of the disease was stressed by Canadians Macrodimitris and Endler [28], as well as by Talbot et al. (237 type 2 diabetics) [29].

The important role of numerous complications of diabetes [17, 30] in the manifestation of depression was observed by English investigators Robinson et al. [31] in a group of patients with type 1 and 2 diabetes mellitus, as well as by Bailey [32] in a group of 180 patients aged 21–81 years.

Haire-Joshu et al. [33] mention the significance of the addiction to smoking in their analysis of 83 smoking and 103 non-smoking diabetic patients.

Egede and Zheng [34] confirmed that age under 65 years, female sex, single status, a period elapsed from diabetes mellitus onset lower than 5 years, coexistence

of complications, addiction to smoking, a poor state of health and poor economic conditions are independent depression risk factors in patients suffering from diabetes mellitus.

Some of these factors are also present in the population free from diabetes [35, 36]. A relationship was established between depression and a younger age, female sex, a low income, a bad somatic state and addiction to smoking [37].

Contrary to previous investigations, the study conducted by Egede and Zheng [34] did not prove a relationship between depression and the presence of numerous complications of diabetes [17, 30–32], unemployment [18, 29], marital status [16, 19, 23], the kind of antidiabetic treatment [38], a low educational status [22, 38] or the duration of diabetes [29].

It seems that the disease itself and its impact on the patient's own sense of health, and not the chronic character or the type of the disease, plays a role in the development of depression. It has been confirmed that metabolic control of diabetes [28], the ensuing day-to-day burden [25] and the fear of the disease [39] are factors significantly related with the development of depression in diabetic patients.

By examining the factors that play a role in the development of depression in Americans of Latin and European origin suffering from diabetes, Fisher et al. [40] noticed that disabilities resulting from diabetes are the strongest anxiety and depression risk factors among the disease-related factors, for both ethnical groups. None of the two biologically dependent variables, HbA_{1c} (glycosylated hemoglobin) and BMI (body mass index), was a significant predictor of depression or anxiety in patients of Latin or European origin. The correlations between these two variables and depression were not significant either.

A number of studies indicate that, compared to a healthy control group, the incidence of depression is high in patients with other chronic diseases as well, such as cardiovascular diseases, asthma and rheumatoid arthritis.

Common cardiovascular diseases and obesity are strongly related with depression and diabetes mellitus. Nichols and Brown [41] made an attempt to answer the question whether depression truly accompanies diabetes mellitus, or it is an effect of the connection of diabetes with comorbidities. In a large population study they observed that depression was about 1.5 times more present in patients with diabetes, compared to a control group of similar sex and age, consisting of patients suffering from cardiovascular diseases and persons with obesity. Depression appeared approximately two times more often in women than in men, independent of the advancement of diabetes. Patients with a diagnosis of depression were younger, and the mean body mass was higher in women. The presence of cardiovascular diseases was the strongest risk factor of depression in diabetic men, while in women it was the body mass.

Finkelstein et al. [42] found a similar difference (1.6 times) in the incidence of depression in the elderly (over 65 years of age) with and without diabetes mellitus.

One of the theories concerning the relationship between depression and diabetes mellitus states that depression may be a factor influencing the development of hyperglycaemia and the increase of the complications risk. Mechanisms through which depression increases the risk of type 2 diabetes development and aggravates its course are unclear. Incorrect behavior, such as non-compliance with the prescribed diet and medical recommendations, smoking or lack of exercise is often induced in the course of depression [38, 43].

However, is the impact of depression on diabetes mellitus fully explained by behavioral factors alone?

Other factors connected with depression, such as a perturbation of glucocorticoid regulation, increased activity of the sympathetic system and decreased immunity, may also play a role in the development of the resistance to insulin [44, 45].

In the Epidemiologic Catchmeat Area (ECA) study of 13 years duration, Eaton et al. demonstrated that depression may be a risk factor of the development of type 2 diabetes mellitus [38].

Other investigators, inspired by Eaton's results, including Carnethon et al., Arioyo et al., Gulden et al. and finally Lustman et al., presented numerous proofs for the effect of depression increasing the risk of the development of type 2 diabetes mellitus.

Reports about the adverse effect of depression on the course of diabetes, as well as of an elevated risk of the development of the disease, provoked another question: does the treatment of depression reduce the risk of diabetes mellitus and its complications?

Lustman et al. demonstrated in a metaanalysis that the degree of diabetes control improved with the treatment of depression, and a decrease in the intensity of depression was related to a better control of glycaemia [44, 46, 47].

Studies conducted so far did not provide unequivocal proofs either for the etiology of both coexisting diseases, or for the relationship between depression and the disease factors accompanying diabetes.

The importance of mental disorders and diabetes mellitus, as well as the connection between these two groups of diseases, creates a necessity for further investigations identifying the risk factors of both disorders, as well as for elaborating optimal prophylaxis and treatment standards.

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