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Depression with atypical features in various types of affective disorders

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Summary

Aim. Assessment of atypical symptoms in various types of depressive disorders using the author's questionnaire for symptoms of atypical depression.

Methods. The study involved 70 patients with a diagnosis of depressive episode in the course of recurrent depression, 54 patients with a diagnosis of depressive episode in bipolar disorder (BD) and 58 patients with a diagnosis of dysthymia. To assess the severity of atypical symptoms, the special questionnaire has been elaborated. In each diagnostic group, half of patients had normal body weight, and half were overweight or obese (BMI > 25).

Results. Patients with various types of depression did not differ significantly in terms of clinical and demographic factors. Symptoms of atypical depression such as increased appetite, weight gain and leaden paralysis were more common in women. Patients with bipolar depression had significantly increased symptoms such as hypersomnia (compared with dysthymia), and leaden paralysis (vs. recurrent depression and dysthymia). In overweight and obese patients, the severity of atypical symptoms correlated with body mass index and intensity of depression score on the 17-items Hamilton Depression Rating Scale. In this group, all symptoms of atypical depression were significantly more intense in patients with depression in the course of bipolar disorder.

Conclusions. The results indicate higher prevalence of symptoms of atypical depression in bipolar disorder compared with recurrent depression and dysthymia. They also suggest the interdependency between the symptoms of atypical depression, bipolar disorder and obesity.

Key words: atypical depression, unipolar depression, bipolar depression

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Introduction

The concept of atypical depression was established in the late 1950s, when it was observed that some patients with depression do not respond to conventional treatment with tricyclic antidepressants but improve after the use of monoamine oxidase inhibitors [1]. In the course of depression the typical clinical picture of melancholic depression was not observed. Currently, atypical depression in ICD-10 (International Classification of Diseases, 10th Revision) is placed in the section "other depressive disorders". The DSM-5 (Diagnostic and Statistical Manual, Fifth Edition) in the description of depression (episode of major depressive disorder, recurrent depression, bipolar disorder or dysthymia) requires its atypical specifiers: reactivity of mood + two (or more) out of four features (increased appetite or weight gain, hypersomnia, heaviness of limbs and interpersonal rejection sensitivity) being present on most of the days of the current episode of depression [2].

One of the main symptoms in atypical depression is the reactivity of mood (not observed in melancholic depression). In atypical depression mood is modulated in response to external factors, e.g., the ability to enjoy some experiences is preserved. This means that mood brightens in response to positive events. Reactivity of mood as a criterion should be accompanied by two or more additional symptoms such as:

- hypersomnia (sleeping too much, more than 10 hours per day, at least 3 days in a week for minimum 3 months);
- significant increase in appetite or weight gain: at least 3–5 kg over the last 3 months;
- leaden paralysis (i.e., heavy, leaden feelings in arms or legs; present at least 1 hour per day, 3 days in a week, for 3 months) – feeling of being heavy or lack of energy;
- interpersonal rejection sensitivity

Atypical depression is different than melancholic depression which is characterized by dissatisfaction and/or no reactivity of mood, depressed mood in the morning, early morning awakening, psychomotor agitation or retardation, decreased appetite and/or weight loss. Unlike melancholic depression, in the course of atypical depression there is no excessive guilt. However, atypical depression is accompanied by increased co-occurrence of other mental disorders, such as: social phobia [3], panic disorder [4, 5], somatization [6], bulimia, and obsessive-compulsive disorders [4, 7, 8]. Substance abuse and personality disorders, especially avoidant, dependent or borderline personality, are more frequently diagnosed among people with atypical depression than among people with other types of depression [5, 9]. Atypical symptoms have been observed more frequently in patients with seasonal depression [9].

The prevalence of atypical depression in different studies is in the range of 0.7 to 4% of the general population [5, 9], and among depressed out-patients it is between 22% [6] and 36% [10].

Aim

The aim of this study was to assess the atypical symptoms in different types of depressive disorders using an original questionnaire (prepared by one of the authors), for symptoms of atypical depression.

Material and methods

Study participants

Patients with a diagnosis of depressive episode in the course of recurrent depression, bipolar disorder and dysthymia (in accordance with the criteria of ICD-10 [11] and DSM-IV [12]) were recruited to the study. Patients were recruited from the Department of Psychiatry and Addiction Treatment of the Ludwik Bierkowski Health Care Centre of the Ministry of Interior in Poznan, and in psychiatric clinics in Poznan and Oborniki Wielkopolskie. All patients involved in the project have been treated in the past 12 months and agreed to participate in the study.

Finally, the study included 182 people, aged 18–65 years, with a diagnosis of depressive episode in the course of recurrent depression, bipolar disorder (BD) or dysthymia. 91 patients (71 women and 20 men) were overweight (body mass index (BMI) falling within the range 25–29.99) or obese (body mass index ≥ 30). The study also included 91 patients (73 women and 18 men) with normal weight (BMI less than 25).

Patients suffering from co-morbid somatic diseases, e.g., diabetes, hypertension, cancer and other chronic diseases that required medication, additional immunosuppressive therapy or steroid therapy were excluded from the study. All patients were studied during acute episode of the illness, and the including criterion was the score ≥ 17 points on 17-items Hamilton Depression Rating Scale (HDRS).

Patients included in the study were treated with serotonin reuptake inhibitors (fluoxetine, sertraline, citalopram, and escitalopram). Patients treated with mirtazapine, mianserin or tricyclic antidepressants (currently or in the past) were not included in the study. In some patients diagnosed with bipolar disorder, mood stabilizers were also used (lamotrigine, carbamazepine or lithium carbonate).

The study was approved by the Bioethics Committee of Poznan University of Medical Sciences.

Psychometric assessment

Assessment of the severity of depression was performed using the 17-items Hamilton Depression Rating Scale [13, 14] and the Beck Depression Inventory (BDI) [15]. We gathered information on atypical symptoms during the current episode of depression – so-called reverse vegetative symptoms persisting for at least 3 months. The subjects

were asked about sleep for 10 or more hours a day at least 3 times a week; increased appetite and weight gain of 3–5 kg over the last three months and the feeling of "leaden paralysis" – "being heavy, leaden" for at least an hour a day, and a sense of rejection.

For the assessment of symptoms of atypical depression, the special questionnaire was elaborated. Table 1 shows the scale for quantitative description of symptoms of atypical depression.

Table 1. **Assessment of atypical symptoms in the questionnaire used in the study**

ATYPICAL SYMPTOMS				
Hypersomnia	Leaden paralysis	Increased appetite	Rejection sensitivity	Weight gain
0 – none 1– 3 days/week 2 – most days of the week 3 – every day	0 – none 1 – 3 days/week 2 – most days of the week 3 – every day	0 –none 1 – only in the evenings 2 – afternoons and evenings 3 – all day, and snacking during nights	0 – none 1 – present in relation to the nearest person 2 – present in relations to the friends 3 – strong, prevents social functioning	0 – none 1 – increased body mass up to 3 kg 2 – increased body mass – 3–5 kg 3 – increased body mass – more than 5 kg

Statistical methods

Statistical analysis of the data included quantitative measures such as mean, standard deviation, and percentage. Analysis for atypical features considered the scores of their severity in the range of 0–3. Further analysis was conducted to test the differences between the groups with normal and excessive body weight. For this analysis we used the Mann-Whitney U test or Student's t-test (for variables meeting the criteria for normal distribution). For comparison between various diagnoses, Kruskal-Wallis multiple comparison test was employed. We analyzed the relationship between quantitative characteristics and Spearman's correlation coefficient was used here. The hypotheses were verified at a significance level of $p < 0.05$.

Results

Table 2 shows characteristics of the studied groups with respect to age of onset, duration of illness, family history, BMI and severity of depression as measured by the HDRS and BDI.

Table 2. **Clinical characteristics of the studied groups with respect to age of onset, duration of illness, family history, BMI and severity of depression as measured by the HDRS and BDI**

	Recurrent depression N = 70	Bipolar depression N = 54	Dysthymia N = 58	p
Age of onset	39 ± 10.5	33.8 ± 10.5	37.2 ± 10.8	NS
Duration of illness (years)	9.6 ± 6.4	15 ± 9	11.6 ± 7.7	NS
Family history	73%	50%	71.4%	NS
BMI	26.4 ± 5.2	27.7 ± 6.5	26.9 ± 5.8	NS
Hamilton Depression Rating Scale	24.3 ± 5.3	23.9 ± 5.1	21.6 ± 4.7	NS
Beck Depression Inventory	29.4 ± 6.1	29.4 ± 6.5	26.3 ± 5.9	NS

NS – not significant. The values expressed as percentages or as means and standard deviation (SD)

Diagnostic groups did not differ significantly in terms of these clinical and demographic factors.

Table 3 shows a degree of severity of atypical depression in men and women.

Table 3. **Severity of atypical symptoms in women and men in the study group**

Atypical symptoms	values	Women N = 144	Men N = 38	p
Hypersomnia	0 1 2 3	61.9% 21.8% 14.7% 1.4%	66.6% 23.8% 9.5% 0.0%	0.449
Increased appetite	0 1 2 3	45.1% 35.1% 16.2% 5.6%	71.4% 19% 9.5% 0%	0.002
Leaden paralysis	0 1 2 3	40.8% 21.1% 27.4% 10.5%	66.6% 21.4% 9.5% 2.3%	0.0008
Rejection sensitivity	0 1 2 3	28.8% 36.6% 24.6% 9.8%	40.4% 40.4% 14.2% 4.7%	0.051
increased body mass – 3–5 kg over the last 3 months	0 1 2 3	53.5% 33.8% 11.2% 1.4%	76.1% 14.2% 9.5% 0%	0.016

As shown in the table, atypical depression symptoms such as excessive appetite, weight gain and leaden paralysis were more severe in women.

Table 4 shows severity of symptoms of atypical depression in different diagnostic categories.

Table 4. **Severity of atypical symptoms in different types of affective disorders**

Atypical symptoms	values	Bipolar disorder F31 N = 70	Recurrent depression F33 N = 54	Dysthymia F34 N = 58	p
Hypersomnia	0 1 2 3	42.1% 31.5% 23.6% 2.6%	61.8% 26.3% 11.8% 0%	75.7% 12.8% 10% 1.4%	F31 vs. F34 0.010 F31 vs. F33 0.153 F33 vs. F34 0.658
Increased appetite	0 1 2 3	44.7% 18.4% 28.9% 7.8%	57.8% 21% 17.1% 3.9%	47.1% 45.7% 4.2% 2.8%	F31 vs. F33 0.326 F31 vs. F34 0.499 F33 vs. F34 1.00
Leaden paralysis	0 1 2 3	23.6% 21.0% 47.3% 7.8%	51.3% 25% 15.7% 7.8%	54.2% 17.1% 18.5% 10%	F31 vs. F33 0.012 F31 vs. F34 0.018 F33 vs. F34 1.00
Rejection sensitivity	0 1 2 3	23.6% 34.2% 18.4% 23.6%	30.2% 40.7% 27.6% 1.3%	37.1% 35.7% 18.5% 8.5%	F31 vs. F33 0.278 F31 vs. F34 0.148 F33 vs. F34 1.00
Weight gain – 3–5 kg over the last 3 months	0 1 2 3	47.37% 28.9% 21.0% 2.6%	67.1% 21% 10.5% 1.3%	55.7% 38.5% 5.7% 0%	F31 vs. F33 0.157 F31 vs. F34 0.605 F33 vs. F34 1.00

As shown in the table, in the group of bipolar depression the prevalence of hypersomnia (compared with dysthymia) and leaden paralysis (vs. recurrent depression and dysthymia) is significantly higher.

In the group of 91 people with excessive body weight, severity of atypical symptoms correlated with body mass index and severity of depression as measured by HDRS-17. No relationship in this respect was found in the group of patients with normal body weight. Table 5 shows severity of symptoms of atypical depression in different diagnostic categories in patients with excessive body weight.

Table 5. **Severity of atypical symptoms in patients with increased body weight (BMI ≥ 25) in different types of affective disorders**

Atypical symptoms	Values	Bipolar disorder F31 N = 35	Recurrent depression F33 N = 27	Dysthymia F34 N = 29	p
Hypersomnia	0	15.7%	50%	65.7%	F31 vs. F33 < 0.05 F31 vs. F34 < 0.01
	1	31.5%	26.3%	14.2%	
	2	47.3%	23.6%	17.1%	
	3	5.2%	0%	2.8%	
Increased appetite	0	10.5%	39.4%	17.1%	F31 vs. F33 < 0.05 F31 vs. F34 < 0.05
	1	15.7%	21%	68.5%	
	2	57.8%	31.5%	8.5%	
	3	15.7%	7.8%	5.7%	
Leaden paralysis	0	0%	36.8%	42.8%	F31 vs. F33 < 0.05 F31 vs. F34 < 0.05
	1	21%	31.5%	22.8%	
	2	68.4%	15.7%	17.1%	
	3	10.3%	15.7%	17.1%	
Rejection sensitivity	0	0%	13.1%	31.4%	F31 vs. F33 < 0.05 F31 vs. F34 < 0.01
	1	26.3%	44.7%	25.7%	
	2	31.5%	39.4%	31.4%	
	3	42.1%	2.6%	11.4%	
Weight gain – 3–5 kg over the last 3 months	0	10.5%	50%	17.1%	F31 vs. F33 < 0.05
	1	42.1%	26.3%	71.4%	
	2	42.1%	21%	11.4%	
	3	5.2%	2.6%	0%	

In the group of overweight/obese patients, all symptoms of atypical depression were significantly more frequent in patients with depression in the course of bipolar disorder.

Discussion

The results obtained in this study indicate that some symptoms of atypical depression are more common in bipolar disorder compared with other diagnostic categories studied here. In contrast, in patients with excessive weight, all symptoms of atypical depression are more frequently observed in the course of BD. This is confirmed by the results of studies conducted since the late 1990s, which have demonstrated more frequent occurrence of atypical symptoms in bipolar depression compared with recurrent depression. In the study of Perugi et al. [4] the prevalence of atypical symptoms of depression in bipolar II disorder was 32.5%, and up to 39.5% in the group of so-

called bipolar spectrum. Atypical symptoms were also more frequent in patients with depression in the course of BD than in patients with unipolar depression [16]. Other studies have found that depression with atypical symptoms (according to DSM-IV), is twice as likely to occur in bipolar II disorder, than in the course of recurrent depression [17, 18]. In the Polish DEP-BI study, the most significant atypical symptoms, such as increased appetite and hypersomnia, occurred significantly more frequently in bipolar than unipolar depression [19, 20]. Some authors consider hypersomnia as an important clinical feature of depression in bipolar disorder [21], and some suggest that atypical depression could be considered as a part of broadly defined bipolar spectrum [4, 22–25]. Our results also confirm more frequent occurrence of symptoms of atypical depression in women than in men, observed in other studies [18, 25].

In this study we used a questionnaire elaborated by Grzegorz Buzuk to measure atypical symptoms in order to systematize the collection of information from patients and to further analyze their relationship with other features and symptoms. It is not a standardized scale, but the simplicity of the questionnaire encourages further research into the wider use of this questionnaire. In the present study, using the questionnaire, analyzing atypical symptoms, we have found that hypersomnia appeared significantly more often in patients with bipolar depression and was more pronounced in this diagnostic group. These findings are consistent with previous observations where hypersomnia was found significantly more often in bipolar disorder [16, 26].

In recent years, increased attention has been paid to atypical symptoms as a potential link between obesity and depression. It seems that depression with hyperphagia and hypersomnia more often leads to excessive weight gain than other types of depression [27]. Although relationships between depression and obesity have long been subject of research, the direction of these relationships is not clear: whether depression causes obesity or obesity leads to depression? The evaluation of atypical symptoms of depression seems important, because of the potential association between atypical depression and increased appetite and excessive eating as well as their effects. In the study of Lasserre et al. [28], based on the 5-year observation, it was shown that weight gain in the case of atypical depression occurs not only during acute episode, but continues after improvement of symptoms. It might be associated with later complications of obesity, e.g., cardiovascular disease. All atypical symptoms were more frequent and more severe in obese subjects with depression than in subjects with normal weight. It is consistent with the research of Levitan et al. [27], who noticed that although comorbidity of depression and obesity is frequent, it is only atypical depression which increases the risk of obesity in the general population. It was also shown that only atypical depression is related to the occurrence of metabolic syndrome, and excessive appetite shows the strongest positive correlation in this respect [29].

Among affective disorders, the highest association with obesity has been shown in relation to bipolar disorder. This was proved in McElroy and Keck's [30, 31] ob-

servations who indicated that bipolar disorder is linked to overweight and obesity, including abdominal obesity and that obese people are characterized by increased severity of such symptoms. In some American studies, more than half of patients with BD showed characteristics of overweight or obesity [32]. It was found that 40% of patients with bipolar disorder showed pre-treatment characteristics of overweight or obesity, significantly more than in other psychiatric disorders [33]. Some authors postulate a bidirectional relationship between the BD and obesity, where both states exert synergistic neurotoxic effects [34]. Vannucchi et al. [35] demonstrated that the characteristics of obesity in people with depression correlated with features of bipolarity. In a study conducted in Krakow, obese group achieved significantly higher scores on the Mood Disorder Questionnaire compared with a group of people with normal weight matched for sex and age [36]. In a study of patients with severe obesity, Alciati et al. [37] found that approximately 90% of them showed characteristics of bipolar spectrum.

In the context of relationship between atypical symptoms and both obesity and bipolar disorder, as well as relationships between bipolar disorder and obesity, the results of our study may confirm the existence of interdependence between the symptoms of atypical depression, bipolar disorder and obesity.

Conclusions

1. Symptoms of atypical depression are more frequent among women than men; they are also more frequent in the course of bipolar depression than in other types of depression.
2. In the group of patients with excess body weight, all symptoms of atypical depression were significantly more frequent in patients with depression in the course of bipolar disorder.
3. The results may indicate the existence of interdependence between symptoms of atypical depression, bipolar disorder and obesity.

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