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# Effect of schizophrenia and substance use disorder on depressive symptoms and stressful life events

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## Abstract

**The aim of the study:** The main aim of this study was to examine the mutual effect of schizophrenia and substance use disorder on depression and stress level.

**Material and methods:** The sample comprised a total of 184 participants, including 51 patients with schizophrenia (S), 45 with dual diagnosis (DD), 44 with substance use disorder (SUD) and 44 healthy controls (HC). The Patient Health Questionnaire-9 and the Hamilton Depression Rating Scale were used to measure depressive symptom severity, while the Social Readjustment Rating Scale was used for the assessment of stressful life events.

**Results:** We found a greater main effect of substance use disorder relative to schizophrenia on the severity of depression symptoms and stressful life events. In addition, the observed significant interaction effect for stressful life events suggested that SUD patients experienced their greatest number while HC reported the fewest such incidents. Interestingly, significant links between stressful life events and depressive symptoms emerged in both SUD patients and HC. What is more, disease duration and exacerbations were significantly associated with depressive symptoms in DD and S patients.

**Discussion:** This study demonstrated the effect of schizophrenia and substance use disorders on depressive symptoms and the severity of stress. The relationship between stressful life events and depressive symptom severity was also investigated.

**Conclusions:** Compared to schizophrenia, substance use disorder has a stronger effect on the presence of depression symptoms and the occurrence of stressful life events. The factors modifying depression symptom severity in both schizophrenia groups differ from those found in SUD patients and HC.

**dual diagnosis; schizophrenia; substance use disorder; depression; stress**

## 1. INTRODUCTION

As a mood disorder, depression is characterized by apathy, low mood, and social withdrawal and it is a common comorbidity among patients with schizophrenia, substance use disorders and dual diagnosis (i.e., schizophrenia with substance use disorder [1,2]. High incidence of depressive disorders in these patient popula-

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tions indicates the importance of early recognition and subsequent intervention, thus warranting greatest benefits of different therapeutic strategies [3]. It is also a significant factor in predicting conversion from ultra-high-risk state to first-episode psychosis, poor clinical outcomes, quality of life, and suicide attempts [4,5,6]. Trials of routine treatment for depression hold promise for significant improvement of patient recovery, reduced suicide rates, and decreased patient suffering [4]. It therefore seems essential to shed more light on the mutual effect of schizophrenia and substance use disorders on depressive symptomatology and stress.

Longitudinal studies show that a clinically significant proportion (up to 80%) of patients with psychosis experience a depressive episode, especially in its early phase [7]. Lifetime rates of co-occurrence of depression and substance use disorders range from 50 to 70% [8,9]. In addition, more severe depressive symptoms have been reported in patients with dual diagnosis relative to their non-addicted counterparts; however, available data are inconclusive and require further analyses [2].

Depression should not consider to be a mere comorbidity and as such requires effective treatment to improve outcomes and support prevention [4]. It is a very complex and multidimensional disorder. In schizophrenia, depressive symptoms may be considered prodromal to psychosis, they may constitute an element of its clinical presentation, or they may occur during remission. Their severity typically fluctuates depending on the stage of the disease (early vs. chronic) and its status (acute or post-psychotic [10]). Available data suggests that self-stigma, shame, difficulty regaining trust in one's own thoughts after recovery from delusional beliefs, and poor motivation are core features of depression in schizophrenia [11]. Of note, the presence of depression and suicidal symptomatology in early psychosis seems conducive to the development of later-onset depression and increased suicidal ideation, thus making early recognition and intervention reducing the later risk of worsening symptoms [7].

Substance use disorders may increase the severity and duration of depressive symptoms and the risk of relapse after withdrawal [12,13]. Moreover, symptoms of depression may arise spontaneously as a result of heavy substance use and then subside with abstinence [14,15]. Alcohol use disorder in depression is associated with reduced likelihood of recovery, increased risk of suicide, poorer social functioning, and increased use of healthcare [16]. Depression is associated with future alcohol use and impairment, earlier age of onset of alcohol use disorder, and higher treatment participation [8]. Comorbid psychoactive substance use significantly affects the exacerbation rates in schizophrenia and is linked with its poorer course [17,18], as well as greater intensity of depressive and anxiety symptoms [19,20,21]. The difference between patients with dual diagnosis and schizophrenia in terms of depressive symptomatology is smaller than commonly assumed and largely depends on the applied rating methodology (self-report vs clinician-rated scales [2]). Dual diagnoses patients relapse more frequently, are more suicidal, engage in more criminal activity, and are more frequently homeless and unemployed [22], which can increase the severity of stress.

The term "stress" refers to the nonspecific body reaction to any demand placed upon it to adapt, whether that demand is pleasant or painful [23]. It can affect health in a variety of ways, including changing behavior [24]. The severity of stress may be measured based on the stressful life events across one's lifespan [25]. Those, in turn, can influence the course of the described disorders [24,26]. A stressful life event can be characterized as a situation or occurrence which entails a change in the individual's personal circumstances in a negative or positive way, indicating or requiring a change in their normal lifestyle pattern [25]. Studies suggest an increased number of such significant incidents in the period prior to psychotic exacerbation or first onset [27,28]. Minor stressful events have also been found to predict symptom exacerbation and anxiety [29]. What is more, a relationship between the severity of stress and the use of psychoactive substances has been demonstrated. Exposure to stressful events may be associated with substance use disorders and increase the risk of relapse [24,30].

Stress is associated with the presence of depressive symptoms [31]. In particular, the first depressive episode has been shown to be preceded with exposure to significant stressors [32].

Severely stressful life events can also contribute to recurrence of major depressive episodes [33]. In addition, people with depression are at least 2.5 times more likely to experience a serious adverse life event compared to controls [34]. In turn, schizophrenia patients have been found to report elevated stress levels relative to healthy individuals in terms of depression, domestic satisfaction, and driven behavior [35]. Substance use disorders in schizophrenia is also common, affecting the course of the disease and contributing to greater depression [19,36].

Previous research shows that people with schizophrenia and patients with substance use disorders report greater depressive symptoms and experience more stressful situations. Available data concerning people with dual diagnoses are inconclusive and require further exploration. To the best of our knowledge, this is the first study on the mutual effect of schizophrenia and substance use disorders on depressive symptoms and the severity of stress. Another aim of this research is to estimate the relationship between depressive symptom severity and the number of stressful life events in people with schizophrenia, dual diagnoses, and patients with substance use disorders. A more profound understanding of the complex interrelations underlying these conditions and symptoms is significant for proper diagnosis, effective treatment, and prevention efforts.

## 2. METHODS

### 2.1. Participants

Recruited to the study were a total of 184 participants, including 51 patients with schizophrenia (S; aged 19-65); 45 with dual diagnosis (DD; aged 19-55), 44 with substance use disorders (SUD; aged 20-59); and 44 healthy controls (HC; aged 19-58) matched for age, years of education, and gender. All diagnoses were based on the ICD-10 criteria [37]. DD group was composed of 19 patients with alcohol use disorders, 10 with drug use disorders (9 people using amphetamine and marijuana, 1 person using amphetamine and cocaine), and 16 with both alcohol and drug use disorders (mainly amphetamine and marijuana or amphetamine alone). DD patients were selected based on medical history, psychiatric examination, and a clinical interview based on the ICD-10. All patients were on antipsychotic treatment and were clinically stable.

Inclusion criteria were age between 18 and 65, comprehension of the study procedure, and written consent to participate. Exclusion criteria were neurological conditions, chronic somatic conditions, brain injury, intellectual disability, dementia, and other psychiatric conditions. Upon approval of the Ethics Committee for Research Projects at the Institute of Psychology of the University of Gdańsk (6/2015), the study was conducted in psychiatric and therapeutic clinics.

### 2.2. MEASURES

#### 2.2.1. The Patient Health Questionnaire

The Patient Health Questionnaire-9 (PHQ-9) is used to assess depression severity over the course of the past two weeks [38]. It is composed of 9 items rated on a scale from 0 to 3 (0 – not at all, 3 – nearly every day [39]. The Polish adaptation is characterized by very good reliability ($\alpha$ = 0.88), sensitivity (82%) and specificity (89% [40]).

#### 2.2.2. The Hamilton Depression Rating Scale

The Hamilton Depression Rating Scale (HDRS [41]) contains 21 items describing depression symptoms, whose severity is rated on a scale from 0 to 4 points in 13 of them, and from 0 to 2 points in the remaining 9 ones. It is one of the most widely used clinician-rated depression symptom and course assessment scales [42]. The Cronbach $\alpha$ reliability coefficient is 0.70 [43].

#### 2.2.3. The Social Readjustment Rating Scale

The Social Readjustment Rating Scale (SRRS [25]) is a self-report measure of stress using objectively weighted life change units and the level of the related adaptive demand. In our study, we measured the stressful life events that occurred over the course of the past 12 months. The SRRS comprises a list of 43 events relating to different categories of stress, including both positive (e.g. marriage, marital reconciliation) and negative ones (e.g. jail term, death of a loved one). Each

event is ranked differently, according to degrees of readjustment (the lowest rank is 11 – minor violations of the law; the highest is 100 – death of spouse).

#### 2.2.4. The Positive and Negative Syndrome Scale

The Polish adaptation [44] of the Positive and Negative Syndrome Scale (PANSS [45]), was used to measure schizophrenia symptom severity (positive, negative, and general psychopathology).

### 2.3. Statistical analysis

All statistical analyses were performed with IBM SPSS 28. Continuous variables are described in terms of means (*M*) and standard deviations (*SD*). Normality of the distributions was checked with the Shapiro-Wilk test and calculation of skewness and kurtosis. Skewness and kurtosis values ranging from – 2 to +2 were considered to indicate normal distribution [46]. One-way analysis of variance was used to check differences in age and years of education, and chi squared test to check the differences in gender. Student *t*-test was used to compare the two patient groups with schizophrenia (DD and S) in terms of clinical factors and psychopathological symptoms. In turn, two-way analysis of variance with two factors (first – schizophrenia and non-schizophrenia; second – substance use disorder and non-substance use disorder) was used to examine differences in depression symptoms and stressful life events. The Bonferroni post hoc test was used for inter-group comparisons. Effect sizes of emerging inter-group differences were calculated using Cohen's *d* or $\eta^2$ [47]. In addition, Pearson's *r* coefficient correlation was used to assess the relationships between variables. The *p*-value was set at $p < 0.05$ for all analyses.

## 3. RESULTS

### 3.1. Demographic and clinical characteristics

As shown in Table 1, no between-group differences were found in gender or age. There were no differences between DD and S patients in terms of disease duration, number of exacerbations, or positive, negative, and general psychopathology symptoms.

**Table 1.** Demographic and clinical participant characteristics.

| Variables / Groups | DD (*n* = 45) | S (*n* = 51) | SUD (*n* = 44) | HC (*n* = 44) | *F* / $\chi^2$ / *t* |
|---|---|---|---|---|---|
| Age: *M* (*SD*) | 34.73 (8.48) | 39.31 (11.74) | 30.07 (9.01) | 35.39 (10.11) | 2.03[a] |
| Years of education: *M* (*SD*) | 12.13 (2.72) | 12.24 (2.90) | 11.61 (2.07) | 11.70 (1.81) | 0.74[a] |
| Gender, male / female: *n* (%) | 9 (20.00) / 36 (80.00) | 22 (43.14) / 29 (56.86) | 11 (25.00) / 33 (75.00) | 17 (33.64) / 27 (66.36) | 7.76[b] |
| Illness duration: *M* (*SD*) | 10.64 (7.39) | 12.93 (10.57) | Min-Max: 0-32 | | -1.25[c] |
| Exacerbations: *M* (*SD*) | 10.80 (7.70) | 8.57 (8.83) | Min-Max: 1-30 | | 1.31[c] |
| Positive symptoms in PANSS: *M* (*SD*) | 26.95 (8.37) | 25.887 (8.89) | Min-Max: 7-41 | | 0.56[c] |
| Negative symptoms in PANSS: *M* (*SD*) | 25.05 (8.69) | 27.52 (9.30) | Min-Max: 7-39 | | -1.25[c] |
| General symptoms in PANSS: *M* (*SD*) | 54.95 (13.18) | 54.24 (15.96) | Min-Max: 28-81 | | 0.22[c] |

PANSS – Positive and Negative Syndrome Scale
DD – Dual diagnosis
S – Schizophrenia
SUD – Substance use disorder
HC – Healthy controls
[a] One-way analysis of variance F test
[b] Chi-squared test
[c] Student's t test

### 3.2. Depression symptoms and stressful life events

As shown in Figure 1, both main effects, i.e., the effect of presence of schizophrenia ($F = 5.94$; $p = 0.018$; $\eta^2 = 0.03$) and the effect of presence of substance use disorder ($F = 40.39$; $p < 0.001$; $\eta^2 = 0.18$) proved significant in terms of depression symptoms, while the interaction effect did not. Pairwise comparisons showed that DD patients scored higher than S patients ($p < 0.001$), while both SUD and S patients scored higher than HC ($p < 0.001$ and $p = 0.004$, respectively). No significant differences emerged between DD and SUD patients.

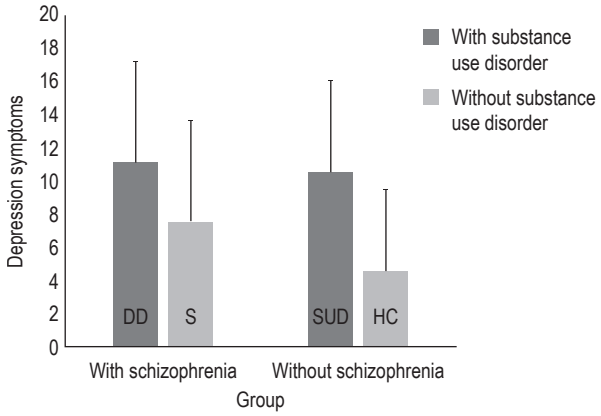


**Figure 1.** Depression symptoms measured with PHQ-9 – Effects of schizophrenia and substance use disorder.

PHQ-9 – Patient Health Questionnaire. DD – Dual diagnosis. S – Schizophrenia. SUD – Substance use disorder. HC – Healthy controls.

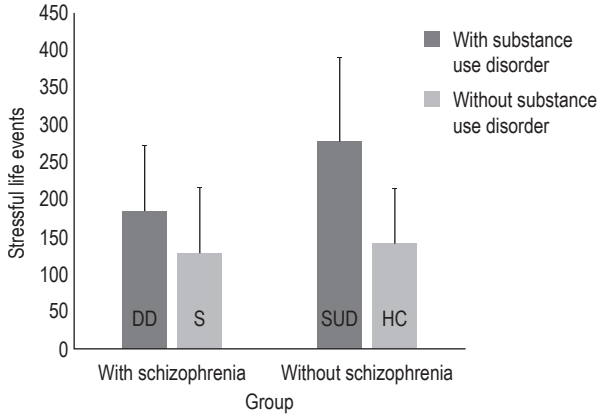


**Figure 2.** Stressful life events measured with SRRS – Effects of schizophrenia and substance use disorder.

SRRS – Social Readjustment Rating Scale. DD – Dual diagnosis. S – Schizophrenia. SUD – Substance use disorder. HC – Healthy controls.

As shown in Figure 2, both the main effects, i.e., the effect of presence of schizophrenia ($F = 16.89$; $p < 0.001$; $\eta^2 = 0.09$) and the effect of presence of substance use disorder ($F = 55.22$; $p < 0.001$; $\eta^2 = 0.24$), and the interaction effect ($F = 9.45$; $p = 0.002$; $\eta^2 = 0.05$) proved significant in terms of stressful life events. Pairwise comparisons showed that DD patients scored higher than S patients ($p = 0.002$), while SUD patients scored higher than both HC ($p < 0.001$) and DD patients ($p < 0.001$). No significant differences were found between S patients and HC.

### 3.3. Relationship between depression symptoms and stressful life events

As presented in Table 2, significant positive correlations emerged between: stressful life events and clinician-rated depression symptoms in SUD patients (HDRS; $p < 0.001$) and stressful life events and self-report depression symptoms in HC (PHQ-9; $p = 0.034$). No significant links between the two variables were found in the two remaining groups (S or DD patients).

**Table 2.** Relationships between depression symptoms and stressful life events in all investigated groups.

| Variables | Stressful life events (SRRS) | | | |
|---|---|---|---|---|
| Depression symptoms | DD | S | SUD | HC |
| Self-reported tool (PHQ-9) | 0.10 | 0.25 | 0.24 | 0.32* |
| Clinician-rated tool (HDRS) | 0.07 | 0.23 | 0.48*** | - |

PHQ-9 – Patient Health Questionnaire
HDRS – Hamilton Depression Rating Scale
SRRS – Social Readjustment Rating Scale
DD – Dual diagnosis
S – Schizophrenia
SUD – Substance use disorder
HC – Healthy controls
* $p < 0.05$ / *** $p < 0.001$

An additional analysis showed significant positive correlations between disease duration ($r = 0.37$; $p = 0.013$ and $r = 0.35$; $p = 0.019$), number of exacerbations ($r = 0.32$; $p = 0.036$) and both self-report and clinician-rated depression symptoms in DD patients. Likewise, significant correlations between disease duration ($r = 0.29$; $p = 0.042$ and $r = 0.32$; $p = 0.026$), number of exacerbations ($r = 034$; $p = 0.014$ and $r = 0.30$;

$p = 0.031$) and depression symptoms measured by both scales were found in S patients.

What is more, significant correlations between self-reported and clinical-rated depressive symptomatology emerged in DD patients ($r = 0.73$; $p < 0.001$), S patients ($r = 0.71$; $p < 0.001$) and SUD patients ($r = 0.74$; $p < 0.001$).

## 4. DISCUSSION

The primary aim of this study was to determine the effect of schizophrenia and substance use disorders on depressive symptoms and the severity of stress. Our results indicate that the occurrence of both substance use disorder and schizophrenia may contribute to greater severity of depression symptoms. Of note, however, based on the size of the main effect, it seems that it is substance use disorder that leads to greater severity of depression symptoms than schizophrenia. In turn, in the absence of a significant interaction effect, we may assume that there was no joint effect of schizophrenia and substance use disorder on the severity of depressive symptomatology. This implies that the specificity of these symptoms in DD patients may therefore be different from one observed in either S or SUD patients, which requires further empirical verification. Due to the paucity of similar studies, it is difficult to compare our results with those of other authors. Inconsistent research results regarding depression symptoms in DD and S patients are presented in a meta-analysis by Potvin et al. [2] while Li et al. [48] did not show a significant difference between these two patient populations in terms of anhedonia.

Nonetheless, research suggests that S patients exhibit symptoms of depression, as they score higher on depression scales compared to HC. Symptoms of depression are common in schizophrenia; with major depression diagnosed in 32.6% of patients [1] and severe symptoms of depression in 39.4% of patients [49]. Depressive disorders are also observed in SUD patients. In their meta-analysis, Conner et al. [8] demonstrated that depressive symptoms are linked with above-average levels of current alcohol use and impairment. The high prevalence of depressive disorders or symptomatology in these patient populations warrants early recognition and subsequent extended intervention efforts [3].

Our study results indicate an increased number of stressful life events in schizophrenia and substance use disorders. As with depressive symptoms, the main effect size for substance use disorder was higher than for schizophrenia, suggesting that groups with SUD experience more stressful life events than participants without SUD. The significant interaction effect demonstrated that schizophrenia and substance use disorder mutually influence the occurrence of stressful life events. SUD patients experience such events to a greater extent than DD patients and HC, and DD patients than S patients alike. Interestingly, S patients did not differ in terms of their occurrence from controls.

Links between stressful life events and substance use disorders have been demonstrated in other studies, with the occurrence of two or more such events significantly increasing the risk of developing a substance use disorder or promoting relapse [50]. DD patients experience more stressful events than S patients and are more likely to use psychoactive substances in stressful situations, which can be explained in terms of maladaptive coping [51]. In turn, the links between stressful events and schizophrenia remain unclear. In their meta-analysis, Beards et al. [52] demonstrated that S patients experience such events slightly more frequently than controls, while Muddle et al. [27] observed no such differences between people at risk of psychosis and HC.

Contrary to expectations, we found no links between stressful events and depressive symptoms in DD or S patients. In turn, such relationships emerged in SUD patients and HC. The nature of depression symptoms in schizophrenia may therefore be construed to be different and determined by factors directly related to the primary condition. Low mood, social withdrawal, anhedonia, and unpleasant thoughts are common in schizophrenia and may be a characteristic feature of the disease itself. Experiencing more stressful life events during the year does not necessarily exacerbate symptoms of depression in people with schizophrenia, regardless of substance use disorder.

A complementary analysis showed that in both schizophrenia groups, a longer disease duration

and a greater number of exacerbations were associated with greater severity of depressive symptoms, as measured by both self-reported (PHQ-9) and clinician-rated tools (HDRS). This remains much in line with other studies, which show that people with schizophrenia and depression report a greater number of exacerbations, are more likely to have a history of depression, and more stressful life events prior to the onset of depressive symptoms [53]. According to Conley et al. [49], individuals with comorbid schizophrenia and depression are more likely to be a safety concern (with more frequent acts of violence, arrests, victimization, suicide risk), report greater substance-related problems, lesser life satisfaction, poorer mental functioning, family relationships, and adherence rates. In another study, compared to healthy controls, schizophrenia patients scored significantly lower on nearly every type of negative or positive events. Apart from the generally lower event frequencies, patients considered the events as generally less controllable and more poorly handled relative to controls and viewed positive events as less desirable [54].

We observed a significant correlation between self-reported and clinical-rated depression symptomatology across all the clinical groups, which may suggest adequate self-assessment and perception of depressive symptoms, consistent with the assessment performed by clinicians in patients with S, SUD, and DD. This is not entirely consistent with the results of a systematic review by Etchecopar-Etchart et al. [1], who showed that S patients indicated greater severity of depressive symptoms on self-report scales relative to clinicians who used clinical-rated tools scales.

Our research has several limitations. Firstly, DD and SUD patients used different psychoactive substances and the specificity of these substances may be associated with depressive symptoms in different ways. Secondly, we did not use screening scales to determine the severity of substance use disorder and cravings. Third, chlorpromazine equivalents were not calculated in both groups of patients with schizophrenia. In future research, it would be worthwhile to check to what extent the severity of depression symptoms and the frequency of stressful life events modify the quality of life and everyday functioning of patients.

## 5. CONCLUSIONS

To conclude, the results of our study indicate that compared to schizophrenia, the presence of substance use disorders may contribute to increased severity of depressive symptoms and is associated with more frequent stressful life events. What is more, SUD patients seem to experience significantly more stressful events than people from other studied groups. The factors modifying the occurrence of depression symptoms in SUD patients and HC are stressful life events, while in DD and S patients it is rather the clinical variables, such as disease duration or number of exacerbations. Self-reported appraisals of depression symptom severity in all three patient groups were consistent with the assessments made by clinicians. Much like previous studies, our results indicate that symptoms of depression and the occurrence of stressful life events are factors that significantly interfere with proper everyday functioning.

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