Psychiatry Research 271 (2019) 195–199

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Identification of risk factors for suicidal ideation in patients with schizophrenia

Fang Xinyu, Chen Yan, Wang Yewei, Zhang Chen*

Schizophrenia Program, Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, Shanghai, PR China

ARTICLE INFO

Keywords:
Schizophrenia
Cognition
Prolactin
Triglyceride
Suicidal ideation

ABSTRACT

Patients with schizophrenia have a high risk for suicide, and therefore, identification of risk factors for suicidal ideation (SI) may be helpful to reduce suicide rate. This study aimed to detect which clinical symptoms and biochemical parameters were most strongly associated with SI. A total of 174 patients and 35 healthy controls were enrolled in our study. Patients were evaluated by the Positive and Negative Syndrome Scale (PANSS), Scale of Assessment Negative Symptoms (SANS) and the Calgary Depression Scale for Schizophrenia (CDSS) for psychiatric and depressive symptoms, and the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) for cognitive function. We examined the levels of prolactin (PRL) and metabolic parameters in all participants. Our results showed a significantly increased level of PRL in patients compared to the controls before ($t = 10.414$, $P < 0.001$) and after ($F = 31.308$, $P < 0.001$) covariates were controlled for. In addition, we found that patients with SI had significantly higher PRL levels than those without SI ($t = 2.586$, $P = 0.011$). And there were positive correlations between serum PRL levels ($r = 0.194$, $P = 0.010$), serum fasting triglyceride levels (TG) ($r = 0.188$, $P = 0.013$), and RBANS visuospatial skill subscores ($r = 0.162$, $P = 0.036$) and SI severity. Finally, the stepwise multiple linear regression analysis revealed that SI severity was significantly associated with PRL levels, fasting TG levels and RBANS visuospatial skill subscores. This study provides support that greater cognitive ability, specifically visuospatial skill, PRL and TG, may confer an elevated risk for more severe SI in schizophrenia patients.

1. Introduction

Schizophrenia is a severe mental disorder with a reduced life expectancy approximately 20 years below that of the general population (Laursen et al., 2014). It has been well established that suicide risk and cardiovascular diseases both play important roles in accelerating mortality in people with schizophrenia (Misiak et al., 2015). The prevalence rate represents an estimated 50% of schizophrenia patients attempting suicide, and up to 13% of suicide deaths are attributable to schizophrenia (Duko and Ayano, 2018). It has been reported that suicidal ideation (SI) is the most powerful predictor of attempted and completed suicide (De Leo et al., 2005; Kessler et al., 2005; Fang et al., 2018). Therefore, identification of its risk factors may be helpful to reduce suicide rates.

The literature has documented the association between suicide risk and demographic characteristics in schizophrenia, including male gender (De Hert et al., 2001), low education levels (Kim et al., 2010), younger age and history of tobacco use (Yan et al., 2013), and clinical features, such as age at onset (Kim et al., 2010), PANSS positive subscale score (Comparelli et al., 2018), cognitive function (Stip et al., 2017), and comorbid depression (Yan et al., 2013). However, in addition to the demographic and clinical associations, accumulating evidence has supported the important role of biochemical markers in predicting suicide risk among schizophrenia.

Hormonal disruption is associated with suicidal risk in various psychiatric disorders (Jose et al., 2015). Additionally, prolactin may play a role in the pathophysiology of schizophrenia. It has been reported that elevated prolactin (PRL) levels are positively associated with suicide risk (Halbreich et al., 2003; Pompili et al., 2012; Pompili et al., 2013), however, there are conflicting results (Jose et al., 2015). New et al. found an association of a blunted PRL response with suicide risk in patients with personality disorder (New et al., 2004).

Metabolic abnormalities caused by various reasons not only increase the risk of cardiovascular disease and lead to death in schizophrenia (Zhang et al., 2017) but also may be related to the risk of suicide. Ainiyet and Rybakowski (2014) revealed a significant association between SI and low total cholesterol (TC), low density lipoprotein cholesterol (LDL), triglyceride (TG) and total lipids in schizophrenia

* Corresponding author.
E-mail address: zhangchen645@gmail.com (C. Zhang).

https://doi.org/10.1016/j.psychres.2018.11.051
Received 29 August 2018; Received in revised form 5 November 2018; Accepted 21 November 2018
Available online 22 November 2018

patients. On the other hand, Huang and Wu (2000) observed no association of serum cholesterol levels with suicide risk in Taiwanese schizophrenia patients.

Due to the contradictory results presented in the past, more research is needed to understand this important issue, exploring symptomatology and biochemical risk factors of suicide in schizophrenia patients. In this study, we aimed to investigate the prevalence of SI in schizophrenia patients and to detect which clinical symptoms and biochemical parameters were most strongly associated with SI. We hypothesized that patients with schizophrenia would have higher PRL levels than those in the controls, and that psychopathological symptoms, the levels of PRL and some metabolic parameters would be significantly associated with SI severity.

2. Methods

2.1. Participants

All schizophrenia patients were recruited from Shanghai Mental Health Center and came from a study that aimed to investigate the neuroimmune mechanisms of depressive symptoms in schizophrenia. Patients were independently diagnosed by two psychiatrists according to the criteria of DSM-IV. Patients were excluded if they met any of the following conditions:(1) had head trauma with residual effects, neurological disorders, or uncontrolled major medical conditions, including any comorbid medical disease that could potentially influence the immune system; (2) had a lifetime substance abuse/dependence disorder; (3) were pregnant or breastfeeding; or (4) had used antidepresssants or mood stabilizers within 1 month prior to study entry. Healthy controls (HC) were recruited from the community and were excluded if they had a history of any Axis I disorder, had a first-degree relative with any Axis I disorder, or had a lifetime substance abuse/dependence disorder. All subjects were Chinese Han who were 18–50 years old and had a junior high school education or above. Written informed consent was obtained from each participant prior to the performance of any procedures related to this study, and all procedures for this study were reviewed and approved by the local ethics committee.

2.2. Clinical evaluation

A questionnaire was applied to collect demographic data from all participants. The Positive and Negative Syndrome Scale (PANSS) and Scale of Assessment Negative Symptoms (SANS) were used for measuring psychopathology exhibited by the schizophrenia patients. The depressive symptoms were assessed with the Calgary Depression Scale for Schizophrenia (CDSS), which is considered to be the best evaluation tool for depression in Chinese patients with schizophrenia (Xu et al., 2018). The patient's cognitive function was evaluated using the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), which included 5 domains of neuropsychological process: (a) immediate memory (list learning and story memory), (b) visuospatial/constructional (figure copy and line orientation), (c) language (picture naming and semantic fluency), (d) attention (digit span and coding), and (e) delayed memory (list learning free recall, list learning recognition, story memory free recall and figure free recall). This instrument works well in cognitive evaluations of patients with schizophrenia (Cai et al., 2015; Zhang et al., 2017) and has good validity and reliability in Chinese people (Cheng et al., 2011). The primary outcome of recent SI was measured on a scale of 0–4 using the suicide item (item 3) from the Hamilton Depression Scale (HAMD). The score represents the severity of recent SI, and only those who answered "0" were defined as without SI, and this cutoff value has been commonly used in previous studies (Ballard et al., 2015; Pu et al., 2015). Patients were subdivided into two groups according to the presence or absence of SI.

All evaluations were conducted by one of the two experienced psychiatrists who were well trained for this project, and an interrater correlation coefficient greater than 0.8 was achieved.

2.3. PRL measurement

Following an overnight fast, serum samples from the patients and healthy controls were collected between 6:00 and 9:00 a.m. and stored at −80 °C until used for the assay. PRL concentration was analyzed in the local hospital biochemistry laboratories using an Access immunoassay analyzer and manufacturer's reagents (Beckman-Coulter Inc., USA). Assay sensitivity was 0.25 ng/ml, and the intra and inter-assay coefficients of variation were <4% and <5%, respectively.

2.4. Metabolic parameters

Metabolic parameters, including fasting TG, high density lipoprotein cholesterol (HDL), LDL, glucose (GLU), and TC, were also examined in the patient group. All of these parameters were measured using an automatic Biochemical Analyzer (HITACHI 7170A, Hitachi, Ltd, Tokyo, Japan) as described in our previous article (Zhang et al., 2014,2017).

2.5. Statistical analyses

Testing for normality was accomplished with the Kolmogorov–Smirnov one-sample test. The comparisons between patients and controls or patients with and without SI in terms of sociodemographic, clinical characteristics and biochemical parameters were performed with the independent Student's *t*-test and Pearson's chi-square test, as appropriate. We further used analysis of covariance (ANCOVA) to control for the effects of confounding variables (age, sex, BMI (body mass index) and years of education) when comparing PRL levels between groups. The correlations between different parameters were calculated by Pearson's correlation analysis. Finally, all demographic and clinical variables that we explored were further analyzed using a stepwise multiple linear regression to assess the association of relative factors with SI, with p values of 0.01 and 0.05 for entry and removal, respectively. Standardized coefficients and 95% confidence intervals (95% CI) were calculated. All tests were two-tailed, and a value of $p < 0.05$ was considered significant. Statistical analysis was performed using the SPSS version 23.0 software package.

3. Results

A total of 174 schizophrenia patients and 35 healthy controls were included in our study. Table 1 presents the demographic characteristics of the patients and controls. There were significant differences in terms

Table 1
Demographic characteristics and serum prolactin levels between schizophrenia patients and controls.

	Schizophrenia $N = 174$	Control $N = 35$	t/χ^2	p
Age (year)	35.83 ± 9.517	41.46 ± 8.385	3.250	0.001
Gender			1.941	0.194
Male	82	12		
Female	92	23		
Education (year)	13.06 ± 8.839	10.49 ± 2.092	11.071	<0.001
Smoking			1.034	0.309
No	154	33		
Yes	20	2		
BMI (kg/m^2)	24.07 ± 3.778	20.49 ± 0.885	1.709	0.089
PRL	2.87 ± 0.537	2.39 ± 0.122	10.414	<0.001

BMI: Body mass index, PRL: Prolactin. Data were presented in Mean ± SD or N.
The difference in serum levels of PRL between patients and controls were still remained after controlled age, gender, BMI and years of education ($F = 31.308$, $P < 0.001$).

Table 2
Differences between patients with and without recent suicidal ideation.

	With SI $N = 26$	Without SI $N = 148$	t/χ^2	P
Age(year)	36.77 ± 9.301	35.67 ± 9.576	0.543	0.588
Gender(male/female)	14/12	68/80	0.554	0.526
Education(year)	13.19 ± 2.871	13.03 ± 9.515	0.084	0.933
Smoking(no/yes)	23/3	131/17	0.000	1.000
Age onset(year)	24.54 ± 6.713	23.48 ± 6.727	0.742	0.459
Course(month)	156.46 ± 91.930	145.11 ± 99.163	0.544	0.587
Episode(first/relapsed)	2/24	7/141	0.396	0.625
Family history(no/yes)	20/6	108/40	0.177	0.811
BMI (kg/m^2)	24.04 ± 3.533	24.07 ± 3.831	0.040	0.968
Antipsychotics (single/combination)	17/9	82/66	0.898	0.395
Fasting GLU (mmol/l)	5.03 ± 0.678	5.43 ± 2.312	0.872	0.384
Fasting TG (mmol/l)	1.70 ± 1.705	1.54 ± 0.936	0.685	0.494
Fasting HDL (mmol/l)	1.15 ± 0.341	1.18 ± 0.304	0.398	0.691
Fasting LDL (mmol/l)	3.15 ± 1.207	2.87 ± 0.826	1.131	0.267
Fasting TC (mmol/l)	4.88 ± 1.493	4.62 ± 1.007	1.098	0.274
Prolactin	3.12 ± 0.427	2.83 ± 0.544	2.586	**0.011**
PANSS				
Positive symptom	12.00 ± 4.378	13.35 ± 4.638	1.358	0.176
Negative symptom	17.00 ± 7.274	16.78 ± 5.996	0.167	0.868
General psychopathology	29.32 ± 6.447	30.75 ± 6.319	1.029	0.311
Total score	58.72 ± 14.173	60.90 ± 12.610	0.785	0.434
SANS				
Affective flattening	15.52 ± 9.395	16.70 ± 10.009	0.573	0.570
Alogia	6.12 ± 6.451	6.48 ± 5.703	0.286	0.775
Avolition	7.48 ± 3.885	7.45 ± 3.498	0.036	0.972
Anhedonia	12.24 ± 5.732	12.01 ± 5.532	0.184	0.855
Attention	2.96 ± 2.922	3.30 ± 3.331	0.486	0.628
Total score	44.60 ± 23.694	44.93 ± 20.693	0.073	0.942
CDSS	5.08 ± 3.37	6.28 ± 3.84	1.494	0.137
RBANS				
Immediate	61.54 ± 13.390	62.16 ± 16.504	0.182	0.856
Visuospatial skill	70.23 ± 11.632	67.30 ± 9.598	1.388	0.167
Language	76.35 ± 18.793	70.18 ± 16.537	1.717	0.088
Attention	89.54 ± 18.500	86.78 ± 16.203	0.782	0.435
Delayed memory	60.38 ± 18.062	58.83 ± 17.824	0.409	0.683
Total score	358.04 ± 63.39	345.17 ± 57.708	1.033	0.303

SI: Suicidal ideation, BMI: Body mass index, GLU: Glucose, TG: triglyceride, TC: total cholesterol, HDL: High density lipoprotein cholesterol, LDL: low density lipoprotein cholesterol. PANSS: Positive and Negative syndrome scale, SANS: Scale of Assessment Negative symptoms. CDSS: Calgary Depression Scale for Schizophrenia. RBANS: Repeatable Battery for the Assessment of Neuropsychological Status. Data were presented in Mean ± SD or N.

of age and years of education between the two groups, while no differences were observed in sex, smoking habits and BMI. The PRL levels in the patient group were nonnormally distributed; however, after taking the logarithmic conversion by log10, the PRL levels in each group were normally distributed (Kolmogorov–Smirnov one-sample test: all $P > 0.05$). We then examined the serum PRL levels between these two groups, and our results showed a significantly increased level of PRL in patients compared to the controls ($t = 10.414$, $P < 0.001$). Although we controlled for covariates such as age, sex, BMI and years of education, this difference still remained ($F = 31.308$, $P < 0.001$) (Table 1).

Among 174 schizophrenia patients, 26 (14.94%) had recent SI. The demographic and clinical characteristics of the patients with and without SI are presented in Table 2. Our results showed that patients with SI, compared to those without, had significantly higher PRL ($t = 2.586$, $P = 0.011$) levels, while there were no significant differences in terms of demographic characteristics, clinical symptoms or metabolic index measures between these two groups (all $P > 0.05$).

Next, we performed correlation analyses to explore whether SI severity in schizophrenia patients was correlated with serum PRL levels and other clinical or biochemical parameters. Our results showed that some biochemical parameters, such as PRL ($r = 0.194$, $P = 0.010$) and fasting TG ($r = 0.188$, $P = 0.013$) levels, and clinical symptoms, such as the RBANS visuospatial skill subscores ($r = 0.162$, $P = 0.036$), were positively correlated with SI severity, while no relationships between other variables and SI severity were found.

Finally, a stepwise multiple linear regression was performed, and the results revealed that SI severity was significantly associated with PRL levels ($\beta = 0.193$, $P = 0.011$), fasting TG levels ($\beta = 0.180$, $P = 0.017$) and RBANS visuospatial skill subscores ($\beta = 0.164$, $P = 0.030$) (Table 3).

4. Discussion

The present study suggested that approximately fifteen percent of patients with schizophrenia had recent SI, which is considered one of the risk factors for suicide in schizophrenic patients (Bakst et al., 2010). The prevalence is similar to the findings of previous studies (Yan et al., 2013), while lower than other studies, which all reported a lifetime prevalence of SI in schizophrenia (Misiak et al., 2015; Dong et al., 2017). It should be mentioned that the relationship between antidepressants and suicide risk is controversial, some researchers have found that antidepressants, especially SSRIs, can increase the incidence of SI (Brent, 2016), while others believe there is no effect or even a reduction in suicide risk from antidepressants (Courtet and Lopez-Castroman, 2017). Therefore, our study excluded patients who were taking antidepressants. In addition, all schizophrenia patients came from a study that aimed to investigate the neuroimmune mechanisms of depressive symptoms in schizophrenia, so we excluded patients who used antidepressants and mood stabilizers within 1 month prior to study entry to avoid the interference of mood-regulating drugs. The difference in the included patients may be the main reason why the rate of SI differed from other studies. However, growing evidence supports the finding that schizophrenia patients have a higher risk of SI than the general population (Forkmann et al., 2012; Cao et al., 2015).

Across the whole sample, we found that patients with schizophrenia had higher levels of serum PRL than controls, and this difference was independent of age, sex, BMI and levels of education. High serum levels of PRL have not only been found in drug-naïve first episode schizophrenia (Song et al., 2014) but have also been reported in patients treated with antipsychotics (Zhang et al., 2002). In our sample, all of the patients used atypical antipsychotic agents, and evidence indicates that most atypical antipsychotic agents produce significantly less

Table 3
Results of the stepwise multiple linear regression analysis: independent risk factors for recent SI in schizophrenia.

Predictors	Unstandardized coefficients		Standardized coefficients			95% CI for exp(B)	
	B	SE		t	p	Lower	Upper
PRL	0.210	0.081	0.193	2.581	0.011	0.049	0.371
TG	0.096	0.040	0.180	2.408	0.017	0.017	0.175
visuospatial	0.009	0.004	0.164	2.191	0.030	0.001	0.018

SI: Suicidal ideation, PRL: prolactin, TG: Triglyceride.

elevation in prolactin than do conventional agents (Casey, 1996). Together with the cross-sectional design of the study, we are unable to draw conclusions whether the increased prolactin levels were caused by antipsychotics or were a manifestation of the disease.

The present study sought a better understanding of SI through blood biochemical parameters. We found elevated serum PRL levels in schizophrenia patients with SI compared to patients without SI, and our correlation and regression analyses showed that serum PRL can serve as an independent risk factor for suicidal ideation in patients with schizophrenia. High levels of serum PRL in schizophrenia patients further proved that schizophrenia have a higher suicide risk than the general population. Interestingly, a cohort study found that suicidal behavior in schizophrenia patients was associated with prolactin-related adverse events (Brugnoli et al., 2012). Additionally, a previous postmortem study confirmed that the mean prolactin levels in cases of suicide was markedly higher than that in nonsuicides (Jones and Hallworth, 1999). It should also be mentioned that early research demonstrated that reduced serotonergic function may be a marker of increased suicide risk in schizophrenia (Correa et al., 2002) and major depression disorder (Correa et al., 2000). In addition, PRL and other hormones may be involved in a complex regulatory mechanism that reduces central serotonin activity (Pompili et al., 2012). Altogether, these findings support the possible involvement of prolactin in the pathogenesis of suicide.

Our results also showed that high levels of fasting TG were a significant risk factor for recent SI in schizophrenia, while no significant association was found in fasting HDL, LDL, TC and GLU. However, Misiak et al. found that only high TC levels, not TG levels, were associated with SI in first episode female schizophrenia (Misiak et al., 2015). In addition, the results of an early study indicated a significant association between SI and low TC, LDL, and TG (Ainiyet and Rybakowski, 2014). Due to the differences in sample sizes and populations included, the exact reasons for these conflicting results are still unknown, and future research is warranted.

Numerous previous studies have examined the relationship between clinical symptoms and suicide risk in schizophrenia with mixed results. Bornheimer et al. found that depression symptoms and positive symptoms of PANSS independently predicted SI in schizophrenia (Bornheimer, 2016). A meta-analysis conducted by Cassidy et al. demonstrated that the PANSS general score and symptoms of depression were higher in patients with SI (Cassidy et al., 2018). Other researchers reported that the PANSS score (including positive, negative and general psychopathology symptoms) (Kim et al., 2010) or depressive symptoms (Gale et al., 2012) were not associated with the risk for suicide in schizophrenia, which was consistent with our study. However, our multivariate analysis showed that RBANS visuospatial skill was positively associated with SI in schizophrenia. Previous studies also suggested that higher cognitive function increases suicide risk in patients with schizophrenia (De Hert et al., 2001; Kim et al., 2003). One mechanistic hypothesis to explain the association between cognitive function and suicide risk is that greater cognitive ability may allow for more effective initiation, planning, mental set-shifting, and goal-directed behavior, thus influencing the patient's ability to initiate and coordinate suicidal behavior (Zoghbi et al., 2014; Villa et al., 2018).

The current study also has several limitations. First, this is a cross-sectional design that could not demonstrate a direct causal link between risk factors and SI in schizophrenia patients. Second, the sample size of patients with SI was relatively small, so the conclusions that can be drawn from our data are limited. Ultimately, future longitudinal research with larger study samples is needed to confirm the hypothesis described above.

In conclusion, a high prevalence of recent SI was found in patients with schizophrenia. Our study confirms that patients with recent SI are characterized by high serum PRL levels, and our study also suggested that serum PRL, fasting TG and RBANS visuospatial skill subscores may predict the risk of SI severity in schizophrenia. These results should be interpreted with caution as contradictory results have been reported previously. However, conflicting results obtained across various studies might be valuable and indicate that SI in schizophrenia might be complex and related to several factors. These factors should be considered in clinical work.

Acknowledgment

The authors thank all the participants. This work was supported by the National Natural Science Foundation of China (81771450, 81471358), the Shanghai Science and Technology Commission Foundation (14411969000), the Shanghai Municipal Education Commission—Gaofeng Clinical Medicine Grant Support (20152530), the Shanghai Municipal Commission of Health and Family Planning Foundation (201540029) and the Shanghai Municipal Commission of Health and Family Planning, Key Developing Disciplines (2015ZB0405).

Conflicts of Interest

None.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2018.11.051.

References

Ainiyet, B., Rybakowski, J.K., 2014. Suicidal behavior in schizophrenia may be related to low lipid levels. Med. Sci. Monit. 20, 1486–1490.
Bakst, S., Rabinowitz, J., Bromet, E.J., 2010. Antecedents and patterns of suicide behavior in first-admission psychosis. Schizophr. Bull. 36 (4), 880–889.
Ballard, E.D., Patel, A.B., Ward, M., Lamis, D.A., 2015. Future disposition and suicidal ideation: mediation by depressive symptom clusters. J. Affect. Disord. 170, 1–6.
Bornheimer, L.A., 2016. Moderating effects of positive symptoms of psychosis in suicidal ideation among adults diagnosed with schizophrenia. Schizophr. Res. 176 (2-3), 364–370.
Brent, D.A., 2016. Antidepressants and Suicidality. Psychiatr. Clin. North. Am. 39 (3), 503–512.
Brugnoli, R., Novick, D., Haro, J.M., Rossi, A., Bortolomasi, M., Frediani, S., et al., 2012. Risk factors for suicide behaviors in the observational schizophrenia outpatient health outcomes (SOHO) study. BMC. Psychiatry 12, 83.
Cai, J., Zhu, Y., Zhang, W., Wang, Y., Zhang, C., 2015. Comprehensive family therapy: an effective approach for cognitive rehabilitation in schizophrenia. Neuropsychiatr. Dis. Treat. 11, 1247–1253.
Cao, X.L., Zhong, B.L., Xiang, Y.T., Ungvari, G.S., Lai, K.Y., Chiu, H.F., et al., 2015. Prevalence of suicidal ideation and suicide attempts in the general population of China: a meta-analysis. Int. J. Psychiatry Med. 49 (4), 296–308.
Casey, D.E., 1996. Side effect profiles of new antipsychotic agents. J. Clin. Psychiatry 57 (11), 40–45 discussion 46-52.
Cassidy, R.M., Yang, F., Kapczinski, F., Passos, I.C., 2018. Risk factors for suicidality in patients with schizophrenia: a systematic review, meta-analysis, and meta-regression of 96 studies. Schizophr. Bull. 44 (4), 787–797.
Cheng, Y., Wu, W.Y., Wang, J.Q., Feng, W., Wu, X.W., Li, C.B., 2011. Reliability and validity of the repeatable battery for the assessment of neuropsychological status in community-dwelling elderly. Arch. Med. Sci. 7 (5), 850–857.
Comparelli, A., Corigliano, V., Lamis, D.A., Stampatore, L., Girardi, P., Pompili, M., et al., 2018. Positive symptoms and social cognition impairment affect severity of suicidal ideation in schizophrenia. Schizophr. Res. 193, 470–471.
Corrêa, H., Duval, F., Mokrani, M., Bailey, P., Trémeau, F., Staner, L., et al., 2000. Prolactin response to D-fenfluramine and suicidal behavior in depressed patients. Psychiatry Res. 93 (3), 189–199.
Corrêa, H., Duval, F., Mokrani, M.C., Bailey, P., Trémeau, F., Staner, L., et al., 2002. Serotonergic function and suicidal behavior in schizophrenia. Schizophr. Res. 56 (1-2), 75–85.
Courtet, P., Lopez-Castroman, J., 2017. Antidepressants and suicide risk in depression. World Psychiatry 16 (3), 317–318.
De Hert, M., McKenzie, K., Peuskens, J., 2001. Risk factors for suicide in young people suffering from schizophrenia: a long-term follow-up study. Schizophr. Res. 47 (2-3), 127–1234.
De Leo, D., Cerin, E., Spathonis, K., Burgis, S., 2005. Lifetime risk of suicide ideation and attempts in an Australian community: prevalence, suicidal process, and help-seeking behaviour. J. Affect. Disord. 86 (2-3), 215–224.
Dong, M., Wang, S.B., Wang, F., Zhang, L., Ungvari, G.S., Ng, C.H., et al., 2017. Suicide-related behaviours in schizophrenia in China: a comprehensive meta-analysis. Epidemiol. Psychiatr. Sci. 1–10.
Duko, B., Ayano, G., 2018. Suicidal ideation and attempts among people with severe

mental disorder, Addis Ababa, Ethiopia, comparative cross-sectional study. Ann. Gen. Psychiatry 17, 23.
Fang, X.Y., Zhang, C., Wu, Z.G., Peng, D.H., Xia, W.P., Xu, J.J., et al., 2018. Prevalence, risk factors and clinical characteristics of suicidal ideation in Chinese patients with depression. J. Affect. Disord. 235, 135–141.
Forkmann, T., Brähler, E., Gauggel, S., Glaesmer, H., 2012. Prevalence of suicidal ideation and related risk factors in the German general population. J. Nerv. Ment. Dis. 200 (5), 401–405.
Gale, C., Skegg, K., Mullen, R., Patterson, T., Gray, A., 2012. Thoughts of suicide and stage of recovery in patients with schizophrenia in community mental health care. Australas. Psychiatry 20 (4), 313–317.
Halbreich, U., Kinon, B.J., Gilmore, J.A., Kahn, L.S., 2003. Elevated prolactin levels in patients with schizophrenia: mechanisms and related adverse effects. Psychoneuroendocrinology 28 (1), 53–67.
Huang, T., Wu, S., 2000. Serum cholesterol levels in paranoid and non-paranoid schizophrenia associated with physical violence or suicide attempts in Taiwanese. Psychiatry Res. 96 (2), 175–178.
Jones, T.J., Hallworth, M.J., 1999. Postmortem prolactin as a marker of antemortem stress. J. Clin. Pathol. 52 (10), 749–751.
Jose, J., Nandeesha, H., Kattimani, S., Meiyappan, K., Sarkar, S., Sivasankar, D., 2015. Association between prolactin and thyroid hormones with severity of psychopathology and suicide risk in drug free male schizophrenia. Clin. Chim. Acta. 444, 78–80.
Kessler, R.C., Berglund, P., Borges, G., Nock, M., Wang, P.S., 2005. Trends in suicide ideation, plans, gestures, and attempts in the United States, 1990-1992 to 2001-2003. JAMA 293 (20), 2487–2495.
Kim, C.H., Jayathilake, K., Meltzer, H.Y., 2003. Hopelessness, neurocognitive function, and insight in schizophrenia: relationship to suicidal behavior. Schizophr. Res. 60 (1), 71–80.
Kim, S.W., Kim, S.J., Mun, J.W., Bae, K.Y., Kim, J.M., Kim, S.Y., et al., 2010. Psychosocial factors contributing to suicidal ideation in hospitalized schizophrenia patients in Korea. Psychiatry Investig. 7 (2), 79–85.
Laursen, T.M., Nordentoft, M., Mortensen, P.B., 2014. Excess early mortality in schizophrenia. Annu. Rev. Clin. Psychol. 10, 425–448.
Misiak, B., Kiejna, A., Frydecka, D., 2015. Higher total cholesterol level is associated with suicidal ideation in first-episode schizophrenia females. Psychiatry Res 226 (1), 383–388.
New, A.S., Trestman, R.F., Mitropoulou, V., Goodman, M., Koenigsberg, H.H., Silverman, J., et al., 2004. Low prolactin response to fenfluramine in impulsive aggression. J. Psychiatr. Res. 38 (3), 223–330.
Pompili, M., Serafini, G., Palermo, M., Seretti, M.E., Stefani, H., Angeletti, G., et al., 2013. Hypothalamic pituitary adrenal axis and prolactin abnormalities in suicidal behavior. CNS. Neurol. Disord. Drug Targets 12 (7), 954–970.
Pompili, M., Gibiino, S., Innamorati, M., Serafini, G., Palermo, M., Girardi, P., et al., 2012. Prolactin and thyroid hormone levels are associated with suicide attempts in psychiatric patients. Psychiatry Res. 200 (2-3), 389–394.
Pu, S., Nakagome, K., Yamada, T., Yokoyama, K., Matsumura, H., Yamada, S., et al., 2015. Suicidal ideation is associated with reduced prefrontal activation during a verbal fluency task in patients with major depressive disorder. J. Affect. Disord. 181, 9–17.
Song, X., Fan, X., Zhang, J., Zheng, H., Li, X., Pang, L., et al., 2014. Prolactin serum levels correlate with inflammatory status in drug-naive first-episode schizophrenia. World J. Biol. Psychiatry 15 (7), 546–552.
Stip, E., Caron, J., Tousignant, M., Lecomte, Y., 2017. Suicidal Ideation and Schizophrenia: contribution of appraisal, stigmatization, and cognition. Can. J. Psychiatry 62 (10), 726–734.
Villa, J., Choi, J., Kangas, J.L., Kaufmann, C.N., Harvey, P.D., Depp, C.A., 2018. Associations of suicidality with cognitive ability and cognitive insight in outpatients with Schizophrenia. Schizophr. Res. 192, 340–344.
Xu, Y.M., Li, F., Liu, XB., Zhong, B.L., 2018. Depressive symptoms in Chinese male inpatients with schizophrenia: prevalence and clinical correlates. Psychiatry Res. 264, 380–384.
Yan, F., Xiang, Y.T., Hou, Y.Z., Ungvari, G.S., Dixon, L.B., Chan, S.S., et al., 2013. Suicide attempt and suicidal ideation and their associations with demographic and clinical correlates and quality of life in Chinese schizophrenia patients. Soc. Psychiatry Psychiatr. Epidemiol. 48 (3), 447–454.
Zhang, C., Fang, X., Yao, P., Mao, Y., Cai, J., Zhang, Y., et al., 2017a. Metabolic adverse effects of olanzapine on cognitive dysfunction: a possible relationship between BDNF and TNF-alpha. Psychoneuroendocrinology 81, 138–143.
Zhang, C., Zhang, Y., Cai, J., Chen, M., Song, L., 2017b. Complement 3 and metabolic syndrome induced by clozapine: a cross-sectional study and retrospective cohort analysis. Pharmacogenomics J. 17 (1), 92–97.
Zhang, X.Y., Zhou, D.F., Yuan, C.L., Zhang, P.Y., Wu, G.Y., Shen, Y.C., 2002. Risperidone-induced increase in serum prolactin is correlated with positive symptom improvement in chronic schizophrenia. Psychiatry Res. 109 (3), 297–302.
Zhang, Y., Chen, M.J, Chen, J., Wu, Z.G., Yu, S.Y., Fang, Y.R., et al., 2014. Metabolic syndrome in patients taking clozapine: prevalence and influence of catechol-O-methyltransferase genotype. Psychopharmacology (Berl) 231 (10), 2211–2218.
Zoghbi, A.W., Deshmukh, P.R., Chen, D.C., Xiu, M.H., Tan, Y.L., Yang, F.D., et al., 2014. Cognitive function and suicide risk in Han Chinese inpatients with schizophrenia. Psychiatry. Res. 220 (1-2), 188–192.