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Suicide risk is associated with low levels of platelet serotonin in bipolar I disorder

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Abstract: Suicide is globally recognized as one of the leading causes of death and a major issue for the public health sector. Considering the importance of suicide, this study attempts to correlate decreased platelet serotonin levels with increased suicide risk in bipolar I disorder (BPD I), while also evaluating other risk factors. All patients admitted to the "Prof. Dr. Alexandru Obregia" Clinical Hospital of Psychiatry in Bucharest, Romania, between the June 1st, 2015 and February 16th, 2016 were asked to participate in this study. Those between 18 and 65 years of age, who agreed to participate and whose diagnoses of BPD I were confirmed using the Mini-International Neuropsychiatric Interview were included in the study, leading to a number of 75 patients. Suicide risk was assessed using the SAD PERSONS Scale to quantify current suicide risk factors. Platelet serotonin levels were determined using the IVD ELISA system (LDN GmbH, Germany) on platelet rich plasma per manufacturer protocol. The scores received from applying the SAD PERSONS Scale were shown to be inversely proportional to platelet serotonin levels, and those patients with bipolar disorder classified as showing medium-high suicide risk, had significantly lower platelet serotonin concentrations. In further studies, with a larger sample size, and other improvements further discussed in this article, it may be possible to demonstrate the need to test platelet serotonin levels as part of the biological model of suicide in bipolar disorder.

Key Words: suicide, suicide risk, SAD PERSONS, serotonin, platelet serotonin, bipolar disorder, biomarker .

INTRODUCTION

Suicide is globally recognized as a leading cause of death and a major public health issue [1, 2]. The basis of any efficient suicide prevention strategy starts with identifying suicide risk factors that are contextually relevant and implementing the appropriate interventions that will eliminate respective risk factors [3].

As far as suicide-associated risk factors are concerned, aside from previous suicide attempts, psychopathology is the most important suicide predicting factor, and is strongly correlated with suicidal behaviour [4, 5]. Studies show that most likely 90% of deaths by suicide occur among those with at least one psychiatric disorder [6], more than half of these patients being diagnosed with mood disorders [7]. Major depressive episodes, associated with recurrent depressive disorder or bipolar disorder (BPD) account for about half of the deaths that occur via suicide [8]. According to a recent meta-analysis, suicide rates among patients with BPD reach an average of 164/100.000, about 10 times higher than the general population [9]. More so, 36.3% of the patients with type 1 BPD, respectively 30.1% of the patients with type 2 BPD, had a history of at least one suicide attempt [10]. Acknowledged plans for suicide represent another key suicide risk factor for people suffering from bipolar disorder [11]. Maladaptive cognitive styles, which highly correlate with suicide [12], represent an underlying feature of psychosis, and thus are present in patients suffering from bipolar disorder

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[13]. Female patients with BPD have been noticed to have a higher rate of suicide attempts, while also being less likely to attempt any of the more violent methods [14]. Among men with BPD, on the other hand, rates of death by suicide are significantly higher [15]. The studies that examine the relationship between age and suicide attempts among bipolar disorder patients, have reported that those with past suicide attempts are much younger compared to those with no suicidal behaviour in the past [15]. Those who are single or have been through a divorce are also significantly more at risk for suicide attempts [15]. Moreover, many bipolar depressions are triggered, among other factors, by a lack of social support [16], which may, in turn, lead to an increased suicide risk. A large number of studies have also reported a higher rate of suicide attempts among subjects with bipolar disorder who also have a history of or currently suffer from substance abuse [15]. Likewise, most studies show that physical comorbidities increase the probability of suicide attempts among those that suffer from bipolar disorder [15].

In the past several years, there has been a clear evolution from studying suicide risk factors towards analyzing the way that multiple socio-psychological, neurobiological, and clinical variables contribute to create what is known as suicidal behaviour. The diathesis-stress model proposes the implication of mental disorders [17-19] and psycho-social factors [20] as triggers for suicidal behaviour. According to this model, impulsivity and aggression are independently associated with suicidal behaviour and reduced serotonergic function [21], correlated with reduced levels of hydroxyindol acetic acid (5-HIAA) in the cerebrospinal fluid, platelet serotonin [23, 24], and prolactin's response to fenfluramine [25]. The serotonergic system's role in suicidal behaviour is documented in several studies [26].

Platelets are a promising peripheral tissue for measuring Serotonin or 5-hydroxytryptamine (5-HT) concentrations [27], and platelet 5-HT levels are considered a reliable indicator of presynaptic serotonin activity [28]. The research shows reduced platelet serotonin levels among those who have attempted suicide, compared to those who have not [29-31]. Moreover, patients with suicidal tendencies show lower platelet serotonin levels, comported to the control groups [32-34.]

Considering the research, this current study proposes to determine and compare platelet serotonin levels among patients who suffer from type I bipolar affective disorder, pursuant to the intensity of suicide risk measured by combining the following clinical, psychological, and social demographic factors: gender, age, depression, previous suicide attempt, ethanol abuse, loss of rational thinking, lack of social support, organized plan, no spouse, and medical comorbidities.

MATERIALS AND METHODS

Design

The study protocol was designed in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the "Prof. Dr. Alexandru Obregia" Clinical Psychiatry Hospital in Bucharest, Romania.

All the patients admitted to the "Prof. Dr. Alexandru Obregia" Clinical Psychiatry Hospital with a documented diagnosis of bipolar I disorder between June 1st, 2015 and February 1st, 2016 were asked to participate in the present study. They were presented with an approved informed consent form, they were given enough time to reflect, and all of their concerns were addressed before signing the form.

The inclusion criteria were represented by: age between 18 and 65 years, and a documented diagnosis of bipolar I disorder, confirmed by applying the Mini-International Neuropsychiatric Interview [35]. The exclusion criteria were: the presence of any psychiatric disorder that, in the investigators' opinion, could interfere with the clinical assessments (e.g. organic mental disorders, mental retardation, etc.), any significant physical disability, severe or uncontrolled medical conditions, and maternal status (pregnancy or postpartum).

Participants

Seventy-five patients were finally included in this study, with a mean age of 44.28 ± 11.38 years. Of the total number of participants, 58.7% were females. Most of our patients were in a manic episode (N = 39, 52.0%), 16 (21.3%) were in a depressive episode, 15 (20.0%) were in remission and 5 (6.7%) were in a mixed episode.

Clinical assessments

The Mini-International Neuropsychiatric Interview (MINI) [35] is a short, structured diagnostic interview based on the Diagnostic and Statistical Manual for Mental Disorders (DSM-IV) [36]. In order to confirm the diagnosis of bipolar I disorder among the participants included in the study, we used the Romanian translated version 6.0.0 of the MINI.

The SAD PERSONS Scale [37] is a widely-used instrument for suicide risk assessment [37]. It was developed based on content validity [38] covering both demographic and clinical factors that are associated with increased suicide risk: male gender, years of age less than 19 or over 45, the presence of depression, a previous suicide attempt, excessive alcohol or substance abuse, loss of rational thinking, poor social and familial support, the presence of a physical illness and having an organized plan for suicide [37]. A SAD PERSONS score of at least 5 was considered to reflect a medium-high suicide risk, and a SAD PERSONS score of at least 7 was considered to reflect a high suicide risk [37].

Further data on possible confounding factors and clinical characteristics of the sample were collected using a semi-structured interview, i.e. current medication, smoking status age at onset, illness duration, total number of episodes, number of manic episodes, number of depressive episodes, and number of hospital admissions, respectively.

Laboratory assessments

Blood samples were collected in EDTA tubes for platelet serotonin concentration assessment. First, platelet rich plasma was obtained by centrifugation at 200g for 10 minutes. Subsequently, a platelet pellet was obtained by centrifugation for 10 minutes at 4500g of 200µl platelet rich plasma mixed with 800µl saline buffer. The platelet pellet was suspended in 200µl deionized water and stored frozen below -40˚C. Platelet serotonin concentration was then determined using the IVD ELISA system (LDN GmbH, Germany), per manufacturer protocol, and referred to 10^9 platelets.

Statistical analysis

The Kolmogorov-Smirnov test was used to test for the normality of data distributions. Spearman correlation coefficients were calculated, as SAD PERSONS scores are not continuous. The Mann-Whitney U test and Student's t test were used to test for between groups differences of quantitative data. Levene's test was used assess the differences in variances for continuous data. The χ^2 test was used to test for differences in qualitative data distributions across groups. The IBM Statistical Pack for Social Sciences (SPSS) version 22.0.0.0 was used for statistical analysis.

Table 1. Correlations between platelet rich plasma serotonin concentrations and SAD PERSONS scores in bipolar I patients

	Spearman's rho	p
Platelet serotonin	- 0.296	0.039

RESULTS

The SAD PERSONS scores inversely correlate with platelet serotonin concentrations with a medium effect size (see Table 1).

Furthermore, bipolar patients showing medium-high suicide risk, as classified by their SAD PERSONS score, had significantly lower platelet serotonin concentrations, with a mean difference of 179.60 ng/10^9 platelets (see Table 2).

The analysis of the distributions of the possible confounders showed no significant differences between our two groups (see Table 3).

The analysis of the distributions regarding the clinical characteristics of the sample showed no significant differences between our two groups (see Table 4).

DISCUSSION AND CONCLUSIONS

The current study showed that BPD I patients with a medium-high risk of suicide, as measured by a cumulative score of known clinical and demographical suicide risk factors, had significantly lower levels of platelet rich plasma serotonin compared with BPD I patients with a low suicide risk. As stated in numerous research studies gender, age, depression, previous suicide attempt, alcohol abuse, loss of rational thinking, lack of social support, organized plan, no spouse, and medical comorbidities represent known suicide risk factors for bipolar disorder [8, 10-16]. As the most useful method for combating suicide is prevention, the assessment

Table 2. Differences in platelet rich plasma serotonin concentrations between low and medium-high suicide risk in bipolar I patients

	Low suicide risk patients	Medium-high suicide risk patients	p
Platelet serotonin	537.98 ± 289.99	358.38 ± 255.62	0.026[1]

1 Student's t test.

Table 3. The distributions of possible confounders between the low *vs.* medium-high suicide risk patients

Possible confounder	Low suicide risk patients Mean (SD) / N	Medium-high suicide risk patients Mean (SD) / N	p
Current treatment with mood stabilizers			
Yes	19	26	NS[1]
No	3	4	
Current treatment with antipsychotics			
Yes	20	25	NS[1]
No	2	5	
Current treatment with antidepressants			
Yes	3	11	NS[2]
No	19	19	
Current smoking			
Yes	13	23	NS[2]
No	9	7	

1 Fisher's Exact test, 2 χ^2 test.

Table 4. The distributions of clinical characteristics between the low vs. medium-high suicide risk patients

Clinical characteristics	Low suicide risk patients Mean (SD) / N	Medium-high suicide risk patients Mean (SD) / N	p
Age at onset	30.86 ± 9.36	29.63 ± 8.85	NS[1]
Duration of illness	14.32 ± 10.01	17.07 ± 10.09	NS[1]
Number of lifetime affective episodes	13.82 ± 9.17	17.50 ± 10.13	NS[2]
Number of lifetime manic episodes	5.00 ± 4.76	5.67 ± 5.02	NS[2]
Number of lifetime depressive episodes	5.05 ± 3.75	7.20 ± 5.23	NS[2]
Number of hospital admissions	9.32 ± 8.68	15.80 ± 14.79	NS[2]

1 Student's t test, 2 Mann-Whitney U test.

of well-established risk factors represents a valuable intervention for reducing suicidal behaviour [2]. The SAD PERSONS Scale, of multiple psychometrics used to study suicidality in adults, is regarded as a valid assessment tool for suicide, having the combined qualities of reliability and speed/ease of administration [39]. A recent review of 9 research studies did not find any indication that the SAD PERSONS Scale performed well in the assessment or prediction of suicide or suicidal behaviour in clinical settings [38]. However, we consider that the review's outcome is irrelevant to the current research, as we did not use the SAD PERSONS Scale to predict future suicidal behaviours and our sample does not subscribe to the 9 analysed studies, which mainly included participants presenting self-harm or suicidal behaviour.

Our results are in line with other research studies that found correlations between low serotonin levels and suicide in schizophrenia [40, 41], schizoaffective disorder [36], post-traumatic stress disorder (PTSD) [29] and depression [30, 31, 42]. Opposing our results, one prior review contests the diagnostic and prognostic value of platelet serotonin levels as a suitable biomarker for suicide risk, by arguing small sample sizes, insufficient matching criteria for controls, and non-consideration of comorbidity in the reviewed data. The current study did not reveal any influence of possible confounders like current psychiatric treatment or smoking habits across our subgroups distribution, as shown in Table 3. The aforementioned review acknowledges that the considerable methodological differences between studies, that limit their comparability, cannot yet form a plausible biological model of suicidality [43].

Considering the fact that a number of clinical factors have been reported as associated with suicide attempts in bipolar disorder [44], we decided to analyse if the age at onset, duration of illness, number of total, manic, and depressive lifetime episodes, and number of previous hospital admissions differ in respect to suicide risk. Our results did not show any significant difference relating to these clinical characteristics between the medium-high and low suicide risk subgroups, as shown in Table 4.

Several limitations of the current study need to be addressed. We were unable to use a layered regressive model to weigh the effects of various drugs (considered efficacious in bipolar disorder) or the distinct clinical subtypes (i.e. current type of episode) with low platelet 5-HT, due to a small sample size. Moreover, due to the cross-sectional design of our study, clinical or biological data for predicting future suicidal behaviour was not available.

In conclusion, the results of the current study have shown lower platelet 5-HT levels for participants with a moderate-high risk of suicide compared with those with a low suicide risk in BPD I. Our results are in line with the current research findings that support a low serotoninergic function in relation to suicidal behaviour [29-31, 34, 36, 40-42]. Further research is needed, with better heterogeneity between larger samples and longitudinal designs, in order to reasonably include platelet serotonin in the biological model of suicide in bipolar disorder. Future development of integrative, theoretic constructs and multidisciplinary approaches to taking on suicide risk factors would increase the possibility of their recognition and contribute to new research perspectives and better suicide prevention.

Conflict of interest. The authors declare that there is no conflict of interest.

References

1. Mann JJ, Apter A, Bertolote J, Beautrais A, Currier D, Haas A, Hegerl U, Lonnqvist J, Malone K, Marusic A, Mehlum L, Patton G, Phillips M, Rutz W, Rihmer Z, Schmidtke A, Shaffer D, Silverman M, Takahashi Y, Varnik A, Wasserman D, Yip P, Hendin H. Suicide prevention strategies: a systematic review. JAMA. 2005;294(16):2064-2074.
2. Preventing Suicide: A Global Imperative. Geneva: World Health Organization; 2014. p. 23.
3. Organization WH. Suicide, Preventing: A global imperative. World Health Organization. 2014.
4. Arsenault-Lapierre G, Kim C, Turecki G. Psychiatric diagnoses in 3275 suicides: a meta-analysis. BMC Psychiatry. 2004;4(1):1-11.
5. Hoertel N, Franco S, Wall MM, Oquendo MA, Kerridge BT, Limosin F, Blanco C. Mental disorders and risk of suicide attempt: a national

prospective study. Mol Psychiatry. 2015;20(6):718-726.
6. Harris EC, Barraclough B. Excess mortality of mental disorder. Br J Psychiatry. 1998;173:11-53.
7. Simon RI, Hales RE. The American Psychiatric Publishing textbook of suicide assessment and management: American Psychiatric Pub; 2012.
8. Holma KM, Haukka J, Suominen K, Valtonen HM, Mantere O, Melartin TK, Sokero TP, Oquendo MA, Isometsa ET. Differences in incidence of suicide attempts between bipolar I and II disorders and major depressive disorder. Bipolar Disord. 2014;16(6):652-661.
9. Schaffer A, Isometsa ET, Tondo L, Moreno DH, Sinyor M, Kessing LV, Turecki G, Weizman A, Azorin JM, Ha K, Reis C, Cassidy F, Goldstein T, Rihmer Z, Beautrais A, Chou YH, Diazgranados N, Levitt AJ, Zarate CA, Jr., Yatham L. Epidemiology, neurobiology and pharmacological interventions related to suicide deaths and suicide attempts in bipolar disorder: Part I of a report of the International Society for Bipolar Disorders Task Force on Suicide in Bipolar Disorder. Aust N Z J Psychiatry. 2015;49(9):785-802.
10. Novick DM, Swartz HA, Frank E. Suicide attempts in bipolar I and bipolar II disorder: a review and meta-analysis of the evidence. Bipolar Disord. 2010;12(1):1-9.
11. Jamison KR. Suicide and bipolar disorder. J Clin Psychiatry. 2000;61 Suppl 9:47-51.
12. Wenzel A, Beck AT. A cognitive model of suicidal behavior: Theory and treatment. Applied and Preventive Psychology. 2008;12(4):189-201.
13. Garety PA, Kuipers E, Fowler D, Freeman D, Bebbington PE. A cognitive model of the positive symptoms of psychosis. Psychological Medicine. 2001;31(2):189-195.
14. Perroud N, Baud P, Preisig M, Etain B, Bellivier F, Favre S, Reber N, Ferrero F, Leboyer M, Malafosse A. Social phobia is associated with suicide attempt history in bipolar inpatients. Bipolar Disord. 2007;9(7):713-721.
15. Schaffer A, Isometsa ET, Azorin JM, Cassidy F, Goldstein T, Rihmer Z, Sinyor M, Tondo L, Moreno DH, Turecki G, Reis C, Kessing LV, Ha K, Weizman A, Beautrais A, Chou YH, Diazgranados N, Levitt AJ, Zarate CA, Jr., Yatham L. A review of factors associated with greater likelihood of suicide attempts and suicide deaths in bipolar disorder: Part II of a report of the International Society for Bipolar Disorders Task Force on Suicide in Bipolar Disorder. Aust N Z J Psychiatry. 2015;49(11):1006-1020.
16. Johnson SL. Life events in bipolar disorder: towards more specific models. Clinical psychology review. 2005;25(8):1008-1027.
17. Beautrais AL, Joyce PR, Mulder RT, Fergusson DM, Deavoll BJ, Nightingale SK. Prevalence and comorbidity of mental disorders in persons making serious suicide attempts: a case-control study. Am J Psychiatry. 1996;153(8):1009-1014.
18. Robins E, Murphy GE, Wilkinson RH, Jr., Gassner S, Kayes J. Some clinical considerations in the prevention of suicide based on a study of 134 successful suicides. American journal of public health and the nation's health. 1959;49(7):888-899.
19. Shaffer D, Gould MS, Fisher P, Trautman P, Moreau D, Kleinman M, Flory M. Psychiatric diagnosis in child and adolescent suicide. Arch Gen Psychiatry. 1996;53(4):339-348.
20. Crawford MJ, Kuforiji B, Ghosh P. The impact of social context on socio-demographic risk factors for suicide: a synthesis of data from case-control studies. Journal of epidemiology and community health. 2010;64(6):530-534.
21. Bloom FE, Kupfer DJ, American College of N. Psychopharmacology: The Fourth Generation of Progress : An Official Publication of the American College of Neuropsychopharmacology: Raven Press; 1995.
22. Mann JJ, Arango V, Marzuk PM, Theccanat S, Reis DJ. Evidence for the 5-HT hypothesis of suicide. A review of post-mortem studies. Br J Psychiatry Suppl. 1989(8):7-14.
23. Alvarez JC, Cremniter D, Lesieur P, Gregoire A, Gilton A, Macquin-Mavier I, Jarreau C, Spreux-Varoquaux O. Low blood cholesterol and low platelet serotonin levels in violent suicide attempters. Biol Psychiatry. 1999;45(8):1066-1069.
24. Giurgiuca A, Cozman D. Integrative models of suicide behavior. Romanian Journal of Psychiatry. 2014;XVI(3):76-82.
25. Malone KM, Corbitt EM, Li S, Mann JJ. Prolactin response to fenfluramine and suicide attempt lethality in major depression. Br J Psychiatry. 1996;168(3):324-329.
26. Dilsaver SC, Benazzi F, Rihmer Z, Akiskal KK, Akiskal HS. Gender, suicidality and bipolar mixed states in adolescents. J Affect Disord. 2005;87(1):11-16.
27. Pandey GN. Altered Serotonin Function in Suicide. Annals of the New York Academy of Sciences. 1997;836(1):182-201.
28. Plein H, Berk M. The platelet as a peripheral marker in psychiatric illness. Hum Psychopharmacol. 2001;16(3):229-236.
29. Kovacic Z, Henigsberg N, Pivac N, Nedic G, Borovecki A. Platelet serotonin concentration and suicidal behavior in combat related posttraumatic stress disorder. Prog Neuropsychopharmacol Biol Psychiatry. 2008;32(2):544-551.
30. Mann JJ, McBride PA, Brown RP, Linnoila M, Leon AC, DeMeo M, Mieczkowski T, Myers JE, Stanley M. Relationship between central and peripheral serotonin indexes in depressed and suicidal psychiatric inpatients. Arch Gen Psychiatry. 1992;49(6):442-446.
31. Roggenbach J, Muller-Oerlinghausen B, Franke L, Uebelhack R, Blank S, Ahrens B. Peripheral serotonergic markers in acutely suicidal patients. 1. Comparison of serotonergic platelet measures between suicidal individuals, nonsuicidal patients with major depression and healthy subjects. J Neural Transm (Vienna). 2007;114(4):479-487.
32. Rao ML, Hawellek B, Papassotiropoulos A, Deister A, Frahnert C. Upregulation of the platelet Serotonin2A receptor and low blood serotonin in suicidal psychiatric patients. Neuropsychobiology. 1998;38(2):84-89.
33. Ruljancic N, Mihanovic M, Cepelak I, Bakliza A, Curkovic KD. Platelet serotonin and magnesium concentrations in suicidal and non-suicidal depressed patients. Magnes Res. 2013;26(1):9-17.
34. Spreux-Varoquaux O, Alvarez JC, Berlin I, Batista G, Despierre PG, Gilton A, Cremniter D. Differential abnormalities in plasma 5-HIAA and platelet serotonin concentrations in violent suicide attempters: relationships with impulsivity and depression. Life Sci. 2001;69(6):647-657.
35. Sheehan DV, Lecrubier Y, Harnett Sheehan K, Janavs J, Weiller E, Keskiner A, Schinka J, Knapp E, Sheehan MF, Dunbar GC. The validity of the Mini International Neuropsychiatric Interview (MINI) according to the SCID-P and its reliability. European Psychiatry. 1997;12(5):232-241.
36. Rao ML, Braunig P, Papassotiropoulos A. Autoaggressive behavior is closely related to serotonin availability in schizoaffective disorder. Pharmacopsychiatry. 1994;27(5):202-206.
37. Patterson WM, Dohn HH, Bird J, Patterson GA. Evaluation of suicidal patients: the SAD PERSONS scale. Psychosomatics. 1983;24(4):343-345, 348-349.

38. Katz C, Randall JR, Sareen J, Chateau D, Walld R, Leslie WD, Wang J, Bolton JM. Predicting suicide with the SAD PERSONS scale. Depress Anxiety. 2017.
39. Brown G. Suicide assessment measures for intervention research with adults and older adults: National Institute of Mental Health; [cited 2017 5 May]. Available from: http://www.sprc.org/sites/default/files/migrate/library/BrownReviewAssessmentMeasuresAdultsOlderAdults.pdf.
40. Marcinko D, Pivac N, Martinac M, Jakovljevic M, Mihaljevic-Peles A, Muck-Seler D. Platelet serotonin and serum cholesterol concentrations in suicidal and non-suicidal male patients with a first episode of psychosis. Psychiatry Res. 2007;150(1):105-108.
41. Braunig P, Rao ML, Fimmers R. Blood serotonin levels in suicidal schizophrenic patients. Acta Psychiatr Scand. 1989;79(2):186-189.
42. Pivac N, Jakovljevic M, Muck-Seler D, Brzovic Z. Hypothalamic-pituitary-adrenal axis function and platelet serotonin concentrations in depressed patients. Psychiatry Res. 1997;73(3):123-132.
43. Muller-Oerlinghausen B, Roggenbach J, Franke L. Serotonergic platelet markers of suicidal behavior--do they really exist? J Affect Disord. 2004;79(1-3):13-24.
44. Grunebaum MF, Ramsay SR, Galfalvy HC, Ellis SP, Burke AK, Sher L, Printz DJ, Kahn DA, Mann JJ, Oquendo MA. Correlates of suicide attempt history in bipolar disorder: a stress-diathesis perspective. Bipolar Disord. 2006;8(5 Pt 2):551-557.