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Tryptophan level is related to personality, not to diagnosis or suicidality, in psychiatric inpatients — a pilot study

Authors: Tytus Jacek Koweszko, Jacek Gierus, Anna Zalewska, Mateusz Maciejczyk, Napoleon Waszkiewicz, Małgorzata Tobiaszewska, Agata Szulc

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BRIEF COMMUNICATION

Tytus Jacek Koweszko[1] https://orcid.org/0000-0002-3696-0148, Jacek Gierus[2], Anna Zalewska[3], Mateusz Maciejczyk[4], Napoleon Waszkiewicz[5], Małgorzata Tobiaszewska[6], Agata Szulc[5]

[1]Department of Psychiatry, Faculty of Health Sciences, Medical University of Warsaw, Poland

[2]Strefa Spotkań, Pruszków, Poland

[3]Independent Laboratory of Experimental Dentistry, Faculty of Medicine, Medical University of Bialystok, Poland

[4]Department of Hygiene, Epidemiology and Ergonomics, Faculty of Health Sciences, Medical University of Bialystok, Poland

[5]Department of Psychiatry, Faculty of Medicine, Medical University of Bialystok, Poland

[6]Students' Scientific Group of Psychiatry, Department of Psychiatry, Faculty of Health Sciences, Medical University of Warsaw, Poland

Tryptophan level is related to personality, not to diagnosis or suicidality, in psychiatric inpatients — a pilot study

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Address for correspondence:

dr n. zdr. Tytus Jacek Koweszko

Department of Psychiatry, Faculty of Health Sciences, Medical University of Warsaw
ul. Żwirki i Wigury 61, 02–091 Warszawa, Poland
e-mail: koweszko@gmail.com

Abstract

According to research studies the deficiency of tryptophan is associated with depression and suicidal behaviours. The objective of this study is to identify the impact of tryptophan on psychological portrait in patients hospitalized psychiatrically. This pilot study included 59 participants, aged 19–65, psychiatrically hospitalized. The Adjective Checklist (ACL) was used to identify personality traits of the subjects. Blood specimens were collected and measured for tryptophan, N-formylkynurenine and kynurenine. The Spearman's rho was used to analyse the relation between psychological picture and biochemical measures. The conducted statistical analysis revealed several significant relationships between personality

traits and fluorescence of tryptophan and N-formylkynurenine. No significant correlations between tryptophan levels and suicidality or diagnosis were disclosed. Outcomes are discussed in terms of potential influence of genetic factors, both on personality and tryptophan levels.
Keywords: psychiatry; depression; tryptophan

Introduction

Numerous studies have revealed that there is a strong association between diet and mental health. One of the significant biochemical components of the human diet is tryptophan, an essential α-amino acid used in the biosynthesis of proteins [1]. It is not produced by humans, but obtained only from diet [2]. It has been hypothesized to be the factor influencing functioning of the central nervous system, thus deficiencies of tryptophan can cause a drop in energy levels, depressed mood or even clinical major depressive disorder [3]. Tryptophan participates in the production of serotonin. It is thought to be involved in the production of melatonin, reducing hyperactivity and tension. It also participates in mood regulation and stabilizing the levels of neurotransmitters such as noradrenaline, dopamine and β-endorphins. Some studies show that tryptophan is beneficial to the immune system [4]. Tryptophan is oxidized to n-formylokynurenine and kynurenine [5]. The kynurenine pathway accounts for the catabolism of around 99% ingested tryptophan, that was not used for protein synthesis [6, 7]. It is reported that the dysfunction of kynurenine pathways is associated with psychiatric disorders such as schizophrenia, major depressive disorder and anxiety disorders [8, 9]. Additionally, there is an increasing number of reports regarding the influence of microbiota on wellbeing [10, 11]. Therefore, there is a connection between emotional and cognitive parts of the brain and alimentary canal. Thus, tryptophan is widely hypothesized to take a crucial part in the development of CNS disorders [6, 13].

Gut-brain axis is nowadays considered to play an important role in suicidal impulses. The large study including general population of 42 countries and the elderly population of 34 countries showed that there is a negative correlation between the consumption of tryptophan and the number of suicides [14]. Despite the epidemiological studies, several research indicate the relationship between tryptophan peripheral availability and suicidality [15, 16]. The risk of suicide does not usually arise from a single factor, such as psychiatric diagnosis, which is rather a mediating factor. However, the ones related to personality, addictions and situational factors are significant. Taking that into consideration, the role of tryptophan may not be

obvious. The mere fact of designating tryptophan as a biological marker does not imply its association with suicide.

The objective of this pilot study is to identify a potential relationship between tryptophan and selected clinical variables of patients hospitalized psychiatrically, like psychiatric diagnosis, suicidality, and personality traits. It was initially hypothesized that lower tryptophan levels would be more specific for subjects with mood disorders and increased risk of suicidality. However, the efficacy of tryptophan as a biomarker in clinical settings can be much lower than in general population.

Material and methods

Subjects

The research study included 59 participants, aged 19–65 [mean age = 35.9 (+/– 12.1) years; females n = 28 and males n = 31], psychiatrically hospitalized at the Clinic of Psychiatry of Faculty of Health Sciences, Medical University of Warsaw. The subjects had different psychiatric diagnoses: substance-related and addictive disorders (n = 14), schizophrenia spectrum and other psychotic disorders (n = 11), depressive disorders (n = 14), anxiety disorders (n = 14) and personality disorders (n = 5). The demographic characteristics of the study participants were as follows: 40.7% of the subjects were married, 56% were single or divorced, and 1.7% were widows/widowers; 23.7% were inhabitants of the village, 35.6% were semi-urban inhabitants, and 39% were urban inhabitants; 13.6% of the participants had primary education, 18.6% vocational education, 52.3% secondary education, and 13.6% had higher education.

The study was approved by the Bioethics Committee of the Medical University of Warsaw (approval number KB/79/2015). Patients were informed about the goals and characteristics of the study and signed written consent.

Measures and procedure

The study consisted of two stages. The first one included individual interview to assess patient’s mental health condition and gain demographic data as well as to conduct psychological testing. Each patient was interviewed by a researcher, who was a clinical psychologist. Nosological diagnoses were made according to DSM-5, based on the interview,

observation, medical documentation and psychological assessment. Biological markers were collected by a nursing team. The Columbia Suicide Severity Rating Scale C-SSRS (Risk Assessment Page) was used for suicidality assessment [17]. The researcher completed obligatory C-SSRS training. C-SSRS is a reliable and valid diagnostic tool in the identification of suicide risk. The scale is evidence-supported and is a part of a U.S. national and international public health initiative involving the assessment of suicidality. The researchers used the Adjective Check List (ACL) for psychological assessment. This tool allows to identify personality traits on 37 scales, including control, needs, thematic, transactional analysis, creativity and intelligence scales. The standard version of ACL was used in the study. The scale consists of the list of 300 adjectives, chosen by the subject based on how relatable they are to the subject. ACL is known for high internal consistency and stability in most of the scales. Internal consistency of the subscales, as well as psychometric stability of the Polish version is proved to be satisfactory. All of the 37 subscales were included in analyses; however, only these that significantly correlated with other factors were presented in the article [18, 19]. The second stage of the study included blood sample collection by a trained psychiatric nurse. The specimens were measured for tryptophan. To detect oxidative stress-modified aromatic amino acids (tryptophan, kynurenine and N-formylkynurenine) samples were diluted 1:10 (*v:v*) in 0.1 M H_2SO_4. Fluorescence at 330/415, 365/480, 325/434, and 95/340 nm was analysed [16]. All results were normalized to fluorescence of 0.1 mg/mL quinine sulfate [20].

Exclusion criteria were a history of neurological or organic disorders or any present major medical illness.

Data analysis

The statistics included the non-parametric Spearman's rank correlation coefficient, median test, and Kruskall-Wallis non-parametric ANOVA. The Statsoft STATISTICA 16 software was used for statistical analyses.

Results

Median test (1.027; p = 0.499) didn't show any significant differences between subjects with suicidal actions/ideations in the last month and subjects without suicidal ideations. No significant differences were observed in terms of fluorescence of kynurenine AFU/mg (0.112; p = 0.773) and N-formylkynurenine AFU/mg (1.010; p = 0.315). Kruskall-Wallis non-parametric ANOVA showed no differences in the levels of tryptophan (1.385; p = 0.847), kynurenine (3.982; p = 0.408) and N-formylkynurenine (8.084; p = 0.089) between subjects with different psychiatric conditions

The correlation analysis was conducted in the group of 59 subjects, taking into account the fluorescence of tryptophan, kynurenine and N-formylkynurenine as well as ACL scales. The results revealed correlations between tryptophan levels and several ACL scales: Fav, Com, End, Int, Nur, Agg, P-Adj, CP, NP, AC, A-2 as well as between N-formylkynurenine and ACL Iss scale. No significant correlations were identified between kynurenine levels and ACL values.

The statistically significant results were presented in Table 1.

Table 1. Analysis of Spearman's rho between ACL scales tryptophan levels (n = 59)

Measurement tool		**Tryptophan**	**Kynurenine**	**N-formylkynurenine**
ACL	Number Checked (No. Ckd)	–0.017	0.084	0.184
	Favourable (Fav)	**0.395****	0.034	–0.016
	Unfavourable (Unfav)	–0.259	–0.012	0.082
	Communality (Com)	**0.295***	0.034	–0.056
	Achievement (Ach)	0.188	0.081	–0.028
	Dominance (Dom)	0.072	0.045	–0.057
	Endurance (End)	**0.342***	0.011	–0.148
	Order (Ord)	0.234	–0.024	–0.209
	Intraception (Int)	**0.365****	0.151	–0.049
	Nurturance (Nur)	0.266	0.045	0.056
	Affiliation (Aff)	0.253	0.121	0.063
	Heterosexuality (Het)	0.116	0.082	0.038
	Exhibition (Exh)	–0.180	–0.014	–0.012
	Autonomy (Aut)	–0.180	0.117	0.070
	Aggression (Agg)	**–0.317***	0.007	0.096
	Change (Cha)	–0.147	0.117	0.255
	Succorance (Suc)	–0.214	–0.169	0.014
	Abasement (Aba)	–0.124	–0.107	0.079
	Deference (Def)	0.200	–0.139	–0.110
	Counselling Readiness (Crs)	–0.236	0.129	0.180

Self-Control (S-Cn)	0.177	–0.003	–0.069
Self-Confidence (S-Cfd)	0.127	0.075	–0.008
Personal Adjustment (P-Adj)	**0.303***	0.076	–0.017
Ideal Self (Iss)	0.102	–0.141	**–0.266***
Creative Personality (Cps)	0.233	0.023	–0.026
Military Leader (Mls)	0.191	0.046	–0.003
Masculine (Mas)	0.167	0.033	–0.120
Femininity (Fem)	0.164	0.079	0.126
Critical Parent (CP)	–0.267	0.072	0.117
Nurturing Parent (NP)	**0.296***	–0.035	–0.141
Adult (A)	0.238	0.109	–0.091
Free Child (FC)	0.065	0.111	0.042
Adapted Child (AC)	**–0.315***	0.055	0.187
High Origence – Low Intellectence (A-1)	–0.007	–0.010	0.006
High Origence – High Intellectence (A-2)	**–0.269***	0.194	0.239
Low Origence – Low Intellectence (A-3)	0.254	0.112	–0.063
Low Origence – High Intellectence (A-4)	0.167	0.088	0.029

*p < 0.05; **p < 0.005

Discussion

These results suggest that in clinical conditions tryptophan, kynurenine and N-formylkynurenine do not have to necessarily be informative biomarkers. There were no differences detected in tryptophan, kynurenine and N-formylkynurenine in subjects with different psychiatric diagnoses. In the group of psychiatric patients, the levels of tryptophan, kynurenine and N-formylkynurenine did not differentiate those with suicidal thoughts/behaviours from those without the risk of suicide. This may indicate that tryptophan and it's metabolites' levels do not directly translate into psychiatric conditions. How, then, does one explain the discovered relationships with certain personality traits? According to one study, personality disorders from clusters B and C exhibit links with the gene encoding tryptophan hydroxylase (TPH-2 gene), which regulates serotonin synthesis. The results of this study also showed that individual functional variants of the TPH-2 gene were associated with

the features of emotional instability in people with personality disorders from clusters B and C. The TPH-2 gene is thus associated with differences in emotional regulation [21–26].

In obtained data patients with lower fluorescence of tryptophan are characterized more than others by discouragement, a tendency to deny everything, fear for the future and being easily overwhelmed by life changes. They can also be more dissatisfied with current position and hardly tolerate social pressure [19]. In present study there were no significant correlations detected between personality features, and kynurenine. Only one significant relationship was revealed between N-formylkynurenine and Ideal Self. However, this correlation was weaker than others and Ideal Self was not related to tryptophan levels, which suggests that this relationship is unclear.

Collected data revealed mainly correlations between some personality features and tryptophan levels. An attempt to explain this phenomenon was made by Gutknecht, Jacob et al. [25], suggesting that the gene coding for TPH2 is the rate limiting enzyme in serotonin synthesis pathway. This causes the TPH2 gene variants to be associated with personality traits, especially the ones related to emotional instability, irritability, and depression. However, it is known from studies on mammals that only a small part of tryptophan is involved in these processes, and yet the amount of tryptophan in diet continues to impact these aspects of behaviour [21–26]. Therefore, we are probably dealing with at least two mechanisms influencing regulation of emotions — one related to the general level of tryptophan and the other to the genetic determinants of its synthesis. However, the first of them is probably not a differentiating factor in psychiatric diagnoses or the risk of suicidality.

Conclusions

Results of this study suggest that the level of tryptophan is probably not related to clinical conditions *per se*. It is likely associated with subclinical or non-clinical aspects of behaviour. There is no evidence so far for its direct role in aetiology of disorders. However, specific mechanisms in non-clinical and subclinical context should be investigated on significantly bigger samples.

Limitations of the study

The fluorescence of tryptophan, kynurenine and N-formylkynurenine, the psychiatric diagnoses, suicidal risk, and personality varies over time. Personality and psychiatric

diagnoses may exist for a long time, whereas the level of tryptophan and suicidal risk may fluctuate over time. Therefore, the relationships of tryptophan, kynurenine and N-formylkynurenine with psychiatric diagnoses, suicidal risk, and personality may vary at different time points in subjects. The limitation of the study was the small size of the study group.

Article information

Author contributions

Conceptualization: T.K. and J.G.; methodology: T.K., J.G., A.Z., M.M., N.W. and A.S.; software: T.K. and M.M.; validation: T.K., J.G., M.T. and A.S.; formal analysis: T.K.; investigation: T.K., J.G. and A.Z. and M.M; resources: N.W.; data curation: T.K.; writing — original draft preparation: T.K., J.G. and M.T.; writing — review and editing: A.S., M.T. and N.W.; visualization: T.K.; supervision: A.S.; project administration: T.K. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

The authors declare no conflict of interest.

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