

Psychometric associations of gastrointestinal discomfort in schizophrenia: depression, anxiety, PTSD, childhood trauma, and coping strategies

Aleksander Turek, Natalia Śmierciak, Marta Szwajca, Katarzyna Furman, Wirginia Krzyściak, Bogna Batko, Paulina Donicz, Maciej Pilecki

Abstract

Aim: Increased prevalence and severity of gastrointestinal symptoms have been observed in schizophrenia, post-traumatic stress disorder, depression, and anxiety disorders. This study aimed to investigate associations between depressive, anxiety-related, and trauma-related psychometric characteristics and gastrointestinal discomfort in schizophrenia.

Material and methods: Thirty-six patients with schizophrenia (SCZ) in a stable phase of the illness and 35 healthy controls (CON), aged 18–40 years, completed the following self-report questionnaires: the Gastrointestinal Symptom Rating Scale (GSRS), Beck Depression Inventory-II (BDI-II), State-Trait Anxiety Inventory (STAI), International Trauma Questionnaire (ITQ), and Traumatic Experiences Checklist (TEC). SCZ participants additionally completed the Coping Inventory for Stressful Situations (CISS) and Childhood Trauma Questionnaire (CTQ). The Calgary Depression Scale for Schizophrenia (CDSS) was administered by a psychiatrist.

Results: SCZ and CON did not differ in any GSRS subscale scores. The groups showed different patterns of correlations between the GSRS and other questionnaires. In SCZ, the GSRS total score correlated positively with STAI trait anxiety ($r = 0.55$; FDR-adjusted $p < 0.05$), ITQ Negative Self-Concept ($r = 0.61$; FDR-adjusted $p < 0.05$), BDI-II ($r = 0.48$; $p < 0.01$), and ITQ Re-experiencing Trauma ($r = 0.47$; $p < 0.01$). In SCZ, GSRS Indigestion correlated significantly with multiple ITQ parameters. In CON, the GSRS Abdominal Pain, Diarrhea, and Reflux subscales correlated positively with STAI state anxiety and the STAI total score. In SCZ, the CISS Task-Oriented Style correlated negatively with GSRS Abdominal Pain ($r = -0.51$; $p < 0.01$), while the Emotion-Oriented Style showed trends toward positive correlations with gastrointestinal discomfort.

Discussion: This study may help inform the screening of individuals with schizophrenia who experience gastrointestinal discomfort. The conclusions are limited by the cross-sectional design, small sample size, and potential influence of pharmacotherapy.

Conclusions: Patients with schizophrenia and healthy participants reported comparable levels of gastrointestinal discomfort. In schizophrenia, significant associations were observed between gastrointestinal discomfort and depressive, anxiety-related, and trauma-related symptoms. Further research on associations between gastrointestinal discomfort and psychometric factors in schizophrenia is warranted.

Aleksander Turek¹, Natalia Śmierciak¹, Marta Szwajca¹, Katarzyna Furman¹, Wirginia Krzyściak², Bogna Batko¹, Paulina Donicz¹, Maciej Pilecki¹: ¹ Department of Child and Adolescent Psychiatry and Psychotherapy, Chair of Psychiatry, Faculty of Medicine, Jagiellonian University Medical College, 31-501 Krakow, Poland
² Department of Medical Diagnostics, Jagiellonian University Medical College, 30-688 Krakow, Poland
Corresponding author: Aleksander Turek
Email: aleksander.turek@uj.edu.pl

INTRODUCTION

Schizophrenia is a severe, chronic psychiatric disorder characterised by cognitive impairment, hallucinations, and delusions. The link between gastrointestinal (GI) complaints and mental disorders has been noted since Galen (2nd century CE) [1]. Contemporary research indicates frequent comorbidity between schizophrenia and GI-related conditions or symptoms (e.g., metabolic syndrome, liver disease, IBS, coeliac disease, and isolated GI symptoms) [2–4]. Koizumi et al. found constipation in 36% of patients with schizophrenia, more than half of whom were unaware that they met the clinical criteria [5]. Virtanen et al. reported constipation in 30% and dyspepsia in 23% of patients and linked constipation to clozapine use [6].

Schizophrenia-related brain pathology may influence the perception of GI symptoms, consistent with reports of altered pain perception in this population [7,8]. GI symptoms are also associated with trauma and PTSD; among people with PTSD, the risk of developing any GI disorder reaches 25% [9]. Studies of PTSD prevalence in schizophrenia have yielded heterogeneous estimates (0–57%), with a pooled meta-analytic prevalence of 10.6% [10,11]. The severity of depressive and anxiety symptoms in schizophrenia varies according to illness stage and overall severity [12–14]. In the general population, anxiety and depressive symptoms are more common among individuals reporting abdominal pain when organic GI disease has been excluded by colonoscopy and laboratory tests [15]. These findings are particularly important given the relatively high prevalence of functional gastrointestinal disorders across countries. Sperber et al. reported findings from an internet-based self-report study involving more than 73,000 participants from over 24 countries, more than 40% of whom met the criteria for at least one functional gastrointestinal disorder [16].

Given the reported associations of gastrointestinal disorders and symptoms with schizophrenia, post-traumatic stress, depression, and anxiety, investigating the relationship between GI discomfort and psychometric characteristics may reveal patterns specific to people with schizophrenia. Moreover, numerous studies have suggested altered pain perception in schizophrenia,

which may affect both the perception of gastrointestinal symptoms and their psychological correlates. To the authors' knowledge, no previous study has simultaneously examined gastrointestinal discomfort in relation to anxiety-related, depressive, and trauma-related characteristics in patients with schizophrenia. This study therefore aimed to compare gastrointestinal discomfort between people with schizophrenia and healthy controls and to examine its associations with psychometric measures of anxiety, depression, childhood trauma, and complex PTSD in schizophrenia.

METHODS

The study included 36 patients with schizophrenia (SCZ) and 35 healthy controls (CON), recruited at the Clinical Department of Adult, Child, and Adolescent Psychiatry, University Hospital in Krakow, Poland. SCZ participants were clinically stable and were independently diagnosed by two psychiatrists according to ICD-10 (F20.0–F20.3) and DSM-5 criteria [17]. Participants were aged 18–40 years. Controls were recruited through advertisements on the hospital's social media channels and through direct outreach. All participants were screened according to predefined criteria. Exclusion criteria included any GI or autoimmune disorder, acute infection, a history of microbiota transplantation, recent antibiotic use, or psychoactive substance misuse within the preceding three months.

Patients with schizophrenia received guideline-concordant pharmacotherapy at optimal doses, consistent with American Psychiatric Association recommendations and the current literature. The complete pharmacotherapy regimen in the SCZ group is presented in Figure 1. Controls were carefully assessed to exclude any current psychiatric diagnosis or previous psychological treatment; individuals receiving psychiatric medication or with an active psychiatric diagnosis were excluded from the analyses. Associations between positive and negative symptom severity and GSRS scores were not significant and were addressed in a separate article focusing on the biological correlates of GI symptoms in schizophrenia.

All participants completed the validated Polish version of the Gastrointestinal Symptom Rating Scale (GSRS) [18,19], rated on a 7-point Likert scale (1 = no discomfort; 7 = very severe discomfort), with items grouped into the Reflux, Abdominal Pain, Indigestion, Diarrhea, and Constipation subscales according to the authors' recommendations. Depressive symptoms were assessed using the Beck Depression Inventory-II (BDI-II) [20], anxiety symptoms using the State-Trait Anxiety Inventory (STAI) [21], and trauma-related symptoms using the International Trauma Questionnaire (ITQ) [22] and Traumatic Experiences Checklist (TEC) [23]. In addition, participants in the SCZ group completed the Coping Inventory for Stressful Situations (CISS) and Childhood Trauma Questionnaire (CTQ) [24,25]. The Calgary Depression Scale for Schizophrenia (CDSS) was administered during the clinical evaluation by a specialist psychiatrist trained in its use [26]. Associations with biological parameters and specific schizophrenia symptoms are described in separate articles [27,28].

Incomplete self-reports and self-reports showing an obvious response pattern (e.g., the same response selected for every item in a questionnaire) were excluded from the analysis, resulting in variation in the number of observations across questionnaires. Statistical analyses were performed in R using the tidyverse, psych, and GGally packages [29–32]. Given the non-normal distributions and presence of outliers, non-parametric methods (Wilcoxon tests and Spearman correlations) were used.

The maximum dosages of pharmacotherapeutic agents were assessed according to the manufacturers' recommendations and The Black Book of Psychotropic Dosing and Monitoring [33].

RESULTS

Demographic data are presented in Table 1. The median age was 31 years in the SCZ group (Q25 = 25; Q75 = 36) and 34 years in the CON group (Q25 = 25; Q75 = 37). Fisher's exact test

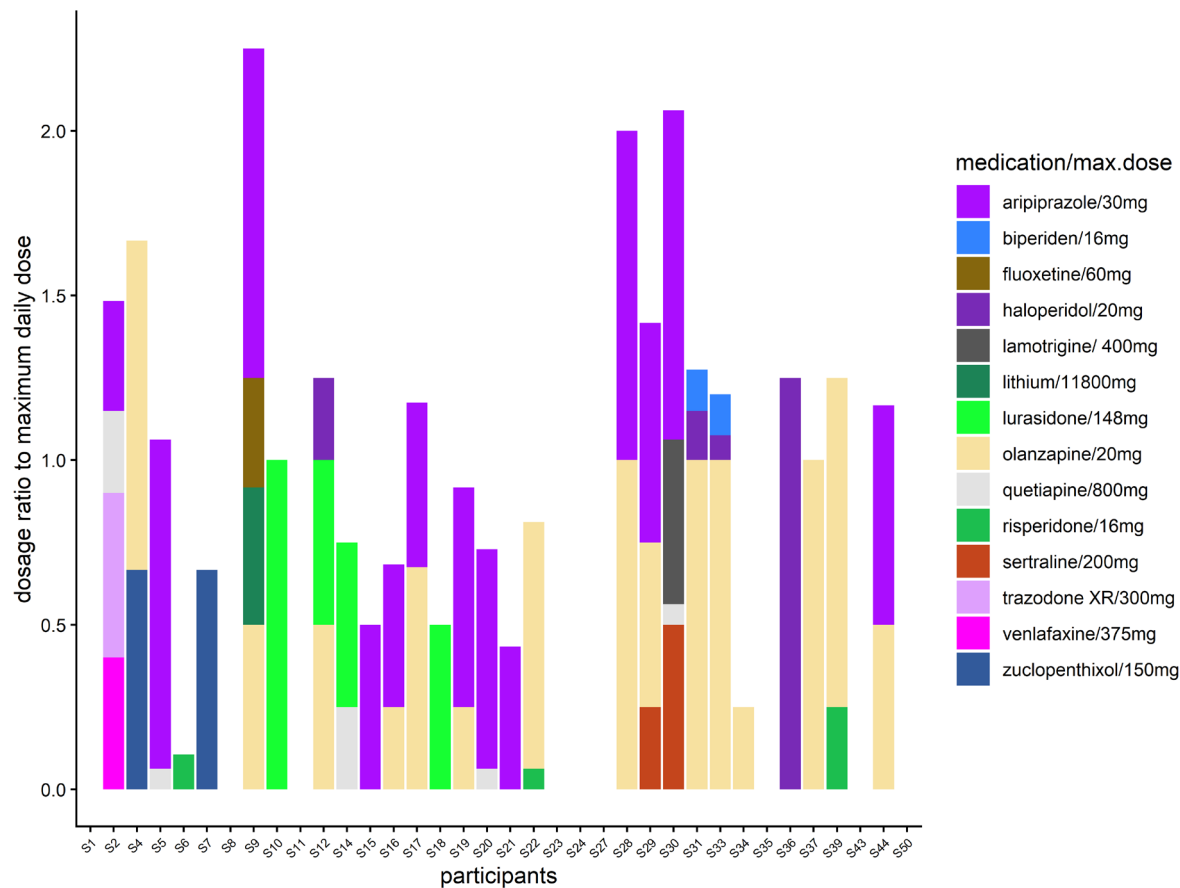


Figure 1. Pharmacotherapy of the SCZ group.

showed significant differences between the groups in sex, education, and employment status.

The results of the intergroup comparisons are presented in Table 2. The groups differed significantly in BDI-II, STAI state anxiety, STAI trait

anxiety, ITQ total score, ITQ Negative Self-Concept, ITQ Disturbance in Relationships, and ITQ Disturbance in Self-Organisation scores.

The results of false discovery rate (FDR)-corrected Spearman rank correlation analyses adjusted for sex are presented in Figures 2 and 3.

Table 1. Demographic characteristics of the CON and SCZ groups, with p-values from Fisher's exact test.

Variable	Category	n-CON	%-CON	n-SCZ	%-SCZ	p
Sex	female	21	60.0	12	33.3	0.033
	male	14	40.0	24	66.7	
Education	primary	0	0.0	1	2.8	0.001
	vocational	2	5.7	5	13.9	
	secondary	7	20.0	20	55.6	
	bachelor	3	8.6	3	8.3	
	master	22	62.9	7	19.4	
	no data	1	2.9	0	0.0	
Residence	town/city	28	80.0	23	63.9	0.109
	village	6	17.1	13	36.1	
	no data	1	2.9	0	0.0	
Professional activity	not employed	0	0.0	9	25.0	0.003
	self-employed	5	14.3	0	0.0	
	full-time job	13	37.1	11	30.6	
	part-time job	3	8.6	3	8.3	
	protected employment	1	2.9	1	2.8	
	odd jobs	4	11.4	3	8.3	
	voluntary job	0	0.0	2	5.6	
	unemployed	2	5.7	7	19.4	
	no data	7	20.0	0	0.0	

Table 2. Intergroup comparisons

Variable	Group	n	Mean	SD	Median	Q0.25	Q0.75	t	p (t)	W	p (W)
BDI	CON	35	7.9	6.7	6.0	2.0	12.5	-3.58	0.001	384	0.005
	SCZ	36	17.2	14.1	13.0	5.0	26.8				
STAI-total	CON	34	75.9	17.1	76.5	66.5	83.8	-3.84	<0.001	316	0.001
	SCZ	36	94.7	23.6	94.0	81.2	109.2				
STAI-state	CON	34	36.7	8.3	35.0	31.0	42.5	-3.97	<0.001	307	<0.001
	SCZ	36	46.4	11.9	47.0	38.8	53.2				
STAI-trait	CON	34	39.2	10.5	40.0	34.2	44.0	-3.12	0.003	334	0.001
	SCZ	36	48.3	13.7	49.0	40.0	56.0				
ITQ-Reexp. Trauma	CON	30	2.6	1.8	2.5	1.0	4.0	-0.19	0.851	521	0.963
	SCZ	35	2.7	2.1	3.0	1.0	4.0				

Variable	Group	n	Mean	SD	Median	Q0.25	Q0.75	t	p (t)	W	p (W)
ITQ-Avoidance	CON	30	3.1	1.8	3.0	2.0	4.0	-0.61	0.545	497	0.714
	SCZ	35	3.4	2.5	3.0	2.0	5.5				
ITQ-Threat	CON	30	3.5	2.4	3.5	2.0	5.0	-0.78	0.440	470	0.472
	SCZ	35	4.0	2.5	4.0	2.0	6.5				
ITQ-Affective Disregulation	CON	30	3.3	1.6	3.5	2.0	4.8	-1.69	0.097	410	0.128
	SCZ	35	4.1	2.1	4.0	2.0	5.5				
ITQ-Negative Self-Concept	CON	30	2.0	1.6	2.0	1.0	3.0	-2.86	0.006	372	0.041
	SCZ	35	3.6	3.0	2.0	2.0	6.5				
ITQ-Disturbance in Relationships	CON	30	2.5	2.1	2.0	0.2	4.0	-2.60	0.012	348	0.019
	SCZ	35	4.0	2.5	4.0	2.0	6.0				
ITQ-PTSDFI	CON	30	4.2	4.0	3.5	0.0	6.0	-1.81	0.075	384	0.061
	SCZ	35	5.9	3.6	6.0	3.0	8.5				
ITQ-DSOFI	CON	30	4.0	2.7	3.0	2.0	5.8	-2.06	0.043	398	0.095
	SCZ	35	5.6	3.8	5.0	2.5	9.0				
ITQ-PTSD	CON	30	9.2	4.4	9.5	6.0	12.0	-0.66	0.515	492	0.668
	SCZ	35	10.1	6.4	10.0	5.5	14.5				
ITQ-DSO	CON	30	7.8	4.1	6.5	4.2	10.8	-2.80	0.007	367	0.038
	SCZ	35	11.7	7.1	10.0	7.0	19.0				
ITQ-total	CON	30	25.2	9.6	22.5	19.0	34.0	-2.35	0.022	367	0.038
	SCZ	35	33.4	17.8	31.0	23.0	44.0				
TEC	CON	35	13.2	11.5	11.0	5.0	16.0	-2.42	0.019	366	0.015
	SCZ	32	21.1	14.8	18.5	11.0	31.0				
GSRS-TOTAL	CON	35	30.8	13.1	26.0	21.5	37.0	0.18	0.855	624	0.954
	SCZ	36	30.3	12.1	27.5	22.0	35.0				
GSRS-REFLUX	CON	35	3.6	2.5	2.0	2.0	4.5	0.12	0.906	656	0.748
	SCZ	36	3.6	2.7	2.0	2.0	4.0				
GSRS-ABDOMINAL	CON	35	5.6	2.9	5.0	3.0	7.5	-0.23	0.822	590	0.641
	SCZ	36	5.8	2.7	5.0	4.0	7.0				
GSRS-INDIGESTION	CON	35	10.5	5.5	10.0	6.0	14.0	0.91	0.364	684	0.537
	SCZ	36	9.4	4.6	8.0	6.0	12.0				
GSRS-DIARRHEA	CON	35	4.9	2.7	4.0	3.0	6.0	-0.99	0.324	538	0.271
	SCZ	36	5.6	3.4	4.0	3.0	6.2				
GSRS-CONSTIPATION	CON	35	6.2	4.4	5.0	3.0	8.0	0.26	0.797	657	0.752
	SCZ	36	5.9	3.9	4.0	3.0	7.2				

BDI-II – Beck Depression Inventory-II; STAI – State-Trait Anxiety Inventory; ITQ – International Trauma Questionnaire; Reexp. Trauma – Re-experiencing Trauma; PTSDFI – Post-Traumatic Stress Disorder Functional Impairment; DSOFI – Disturbance in Self-Organisation Functional Impairment; DSO – Disturbance in Self-Organisation; TEC – Traumatic Experiences Checklist; GSRS – Gastrointestinal Symptom Rating Scale; total – total score

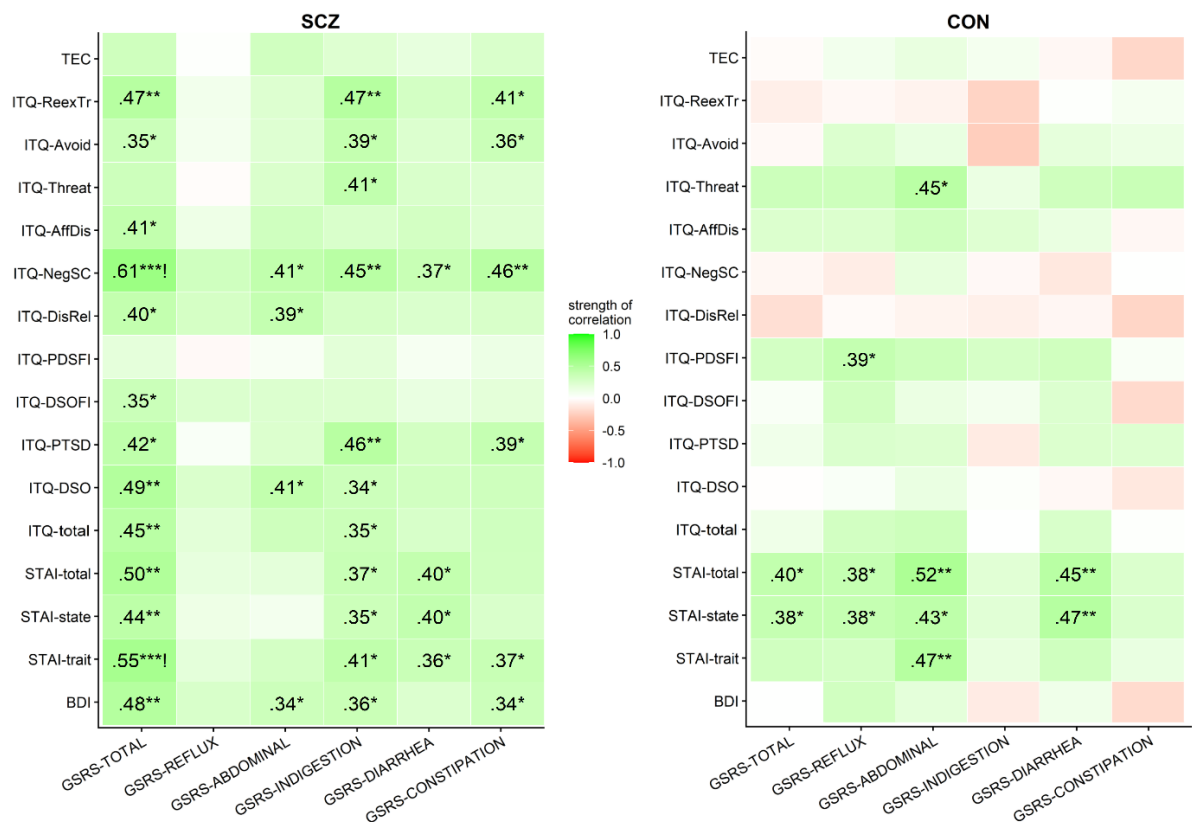


Figure 2. Spearman rank correlation analysis adjusted for sex

* p < 0.05; ** p < 0.01; *** p < 0.001; ! FDR-adjusted p < 0.05

TEC – Traumatic Experiences Checklist; ITQ – International Trauma Questionnaire; ReexTr – Re-experiencing Trauma; Avoid – Avoidance; AffDis – Affective Dysregulation; NegSC – Negative Self-Concept; DisRel – Disturbance in Relationships; PTSDFI – Post-Traumatic Stress Disorder Functional Impairment; DSOFI – Disturbance in Self-Organisation Functional Impairment; PTSD – Post-Traumatic Stress Disorder; DSO – Disturbance in Self-Organisation; STAI – State-Trait Anxiety Inventory; BDI-II – Beck Depression Inventory-II; total – total score. Correlation analyses with and without FDR correction were performed only for variables shown in the figure.

DISCUSSION

The primary finding of this study was that GRSR scores were comparable between patients with schizophrenia and healthy controls—an unexpected result given previous reports suggesting comorbidity between GI disorders and schizophrenia [1–4]. Overall, the literature does not conclusively establish a greater GI symptom burden in schizophrenia, and reported associations often relate to antipsychotic treatment. Research on antipsychotics and the GI system has focused mainly on hypomotility and the gut microbiota. Every-Palmer et al. highlighted potentially life-threatening GI hypomotility associated with clozapine, with little effect of other antipsychotics on motility [34], consistent with clinical observations that constipation is most prominent

in patients treated with clozapine [6]. Interest in the microbiota–gut–brain axis and the antibacterial properties of antipsychotics has stimulated microbiome research, but Dias et al. concluded that the methods are heterogeneous and the findings inconclusive [35,36]. One possible explanation for the present finding is that second-generation antipsychotics may reduce visceral discomfort through mechanisms involving serotonergic (5-HT3/5-HT4) and glutamatergic (NMDA) modulation. Such mechanisms may be related to altered visceral pain perception, as suggested by previous research [37]. However, systematic reviews of pain perception in schizophrenia have yielded mixed findings, including hypoalgesia, hyperalgesia, and no differences; consistent hypersensitivity has been report-

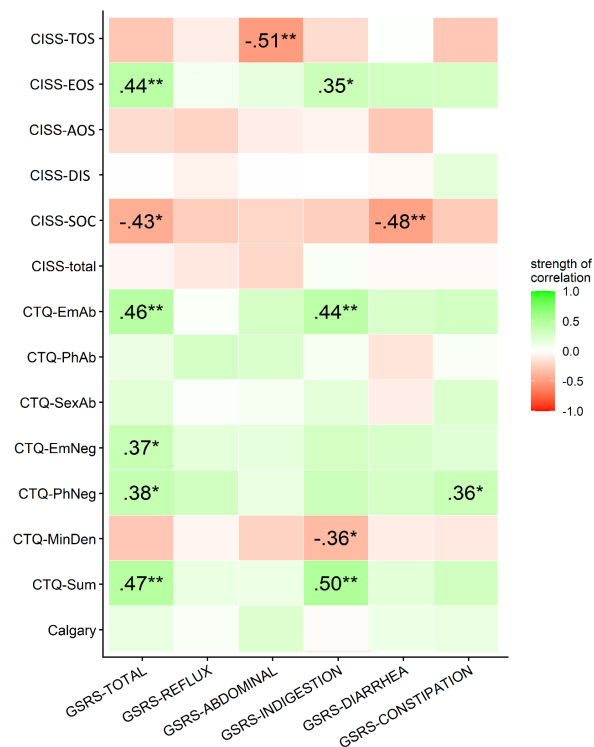


Figure 3. Spearman rank correlation analysis adjusted for sex – SCZ

* p < 0.05; ** p < 0.01

CISS – Coping Inventory for Stressful Situations; TOS – Task-Oriented Style; EOS – Emotion-Oriented Style; AOS – Avoidant-Oriented Style; DIS – Distraction Seeking; SOC – Social Diversion; CTQ – Childhood Trauma Questionnaire; EmAb – Emotional Abuse; PhAb – Physical Abuse; SexAb – Sexual Abuse; EmNeg – Emotional Neglect; PhNeg – Physical Neglect; MinDen – Minimisation/Denial. Correlation analyses with and without FDR correction were performed only for variables shown in the figure.

ed only in a few studies using mechanical pain stimuli [7,8].

Importantly, the GSRs captures subjective bother rather than objective symptom severity (e.g., frequency or stool form). Its wording (“have you been bothered...”) emphasises the emotional burden of symptoms as well as their presence. This distinction is relevant because differences in emotion processing in schizophrenia—such as the misclassification of emotions and altered brain responses to emotional stimuli—have been reported [38]. EEG findings also suggest that psychosis severity, cognition, and psychosocial functioning may shape emotion recognition more strongly than diagnosis alone [39].

Within the schizophrenia group only, BDI-II scores correlated positively with the GSRs total,

Indigestion, and Constipation scores. Depressive symptoms were more severe than in controls, consistent with previous literature [40]. No significant associations were found between the GSRs and negative symptoms [41] or between the GSRs and the CDSS. Although CDSS scores showed trends toward positive associations with all domains of gastrointestinal discomfort, the lack of significant findings contrasts with the significant associations observed for the BDI-II. These results may suggest that the BDI-II has greater convergent validity with the GSRs than the CDSS. Clinically, the BDI-II may therefore be more useful than the CDSS in identifying patients with schizophrenia who are likely to report gastrointestinal discomfort. Anxiety levels were also higher in the schizophrenia group (STAI trait, state, and total scores), while both groups showed broadly similar patterns of correlations between the GSRs and STAI. The association between state anxiety and diarrhoea is consistent with findings from large population studies [15]. Differences between the groups in associations involving the GSRs Abdominal Pain subscale (upper abdominal discomfort, hunger pains, and nausea) and Indigestion subscale (rumbling, bloating, belching, and flatulence) are relevant to the interpretation of these patterns [18,19]. Importantly, the positive association between overall gastrointestinal discomfort and trait anxiety remained significant after FDR correction only in the SCZ group.

Trauma-related characteristics appear to be associated with gastrointestinal discomfort in a manner that may be specific to schizophrenia. In the International Trauma Questionnaire, Re-experiencing Trauma correlated with the GSRs Abdominal Pain and Constipation subscales only in schizophrenia, despite the absence of a between-group difference in Re-experiencing Trauma scores. Negative Self-Concept showed the most pronounced pattern: the associations remained significant after FDR correction, and this domain correlated positively with multiple GSRs subscales only in schizophrenia. Negative Self-Concept scores were also significantly higher and more dispersed in the schizophrenia group than in controls, suggesting the presence of a subgroup with markedly elevated scores. In the authors’ statistical analysis, visual trends in scatterplots indicated that very high Nega-

tive Self-Concept and total ITQ scores clustered among participants with schizophrenia whose BDI-II scores exceeded 25. High Negative Self-Concept scores were related to elevated GSRS total scores only in schizophrenia, whereas some controls reported elevated GSRS scores despite minimal ITQ and BDI-II scores. ITQ PTSD symptom totals correlated with the GSRS Abdominal Pain, Constipation, and total scores exclusively in schizophrenia. These findings are consistent with previous work demonstrating altered pain profiles in combat-related PTSD and associations between pain intensity and anxiety or dissociation in experimental paradigms [42]. Notably, the ITQ Disturbance in Self-Organisation (DSO) score correlated with the GSRS total score only in schizophrenia, particularly with abdominal symptoms, paralleling evidence that DSO is related to IBS symptom intensity in a large clinical sample [43].

Childhood trauma measures yielded less pronounced findings. Total TEC scores did not correlate significantly with gastrointestinal discomfort in either group. On the CTQ, Emotional Abuse was associated with the GSRS total and Indigestion scores. Previous research using the Adverse Childhood Experiences questionnaire has shown that the odds of IBS increase with greater adversity, with emotional abuse and certain household stressors identified as predictors [44]. Other research has found a higher prevalence of traumatic experiences among people with inflammatory bowel disease [45].

The analysis of the CISS results indicates potential associations between particular coping styles and gastrointestinal discomfort. A Task-Oriented coping style was negatively associated with GSRS Abdominal Pain, suggesting that individuals who use problem-solving strategies may experience less abdominal discomfort. Conversely, an Emotion-Oriented coping style showed positive correlations with the GSRS total and Indigestion scores, indicating a trend toward greater gastrointestinal discomfort among individuals who use this coping approach. These findings may be consistent with previous research linking Emotion-Oriented coping to heightened stress responses and poorer quality of life [46].

The main clinical implication of this study is that patients with schizophrenia who have

a pronounced negative self-concept and persistent anxiety may be particularly likely to experience substantial subjective gastrointestinal discomfort. This group may benefit from proactive screening for GI symptoms by healthcare professionals, including psychiatrists and psychotherapists. The findings also suggest a potential benefit of supporting a shift from emotion-oriented coping towards alternative strategies, such as task-oriented coping. Although the exploratory nature of this study does not permit conclusions about medical interventions, addressing gastrointestinal discomfort during psychotherapy sessions, psychiatric consultations, or hospitalisation may potentially improve treatment adherence among patients with schizophrenia.

LIMITATIONS

Both the control (CON) and schizophrenia (SCZ) groups were relatively small, which likely limited statistical power. The correlational design also precludes causal inference: although some variables (e.g., childhood trauma) may suggest directional effects, most findings cannot establish cause-and-effect relationships. For example, the association between ITQ Negative Self-Concept and GSRS scores may be bidirectional, as frequent and distressing GI symptoms could worsen perceived well-being. The results may also have been influenced by significant between-group differences in sex, employment, and education. Adjusting the correlation analyses for sex helped account for the potential influence of sex differences. The authors did not include employment or education as covariates because meta-analyses and nationwide studies indicate that lower educational attainment and high unemployment rates commonly follow a diagnosis of schizophrenia [47,48].

Another limitation is the reliance on self-report measures of psychological factors and GI discomfort. More objective assessments—such as neuropsychological testing of cognition, collateral interviews with family members to assess trauma history, and clinical evaluation of GI symptoms—could strengthen the conclusions. Finally, because the GSRS measures subjective “bother” rather than symptom frequency or objective severity, future studies could include ob-

jective symptom indices, such as stool characteristics, and diagnostic frameworks such as the Rome criteria for IBS to improve the accuracy of assessments of GI–psychological associations.

CONCLUSIONS

Individuals diagnosed with schizophrenia report gastrointestinal discomfort of an intensity similar to that reported by healthy controls. In schizophrenia, gastrointestinal discomfort is associated with symptoms of depression, anxiety, and trauma, as well as with particular emotion-oriented coping strategies. In contrast, healthy participants show mainly an association between gastrointestinal discomfort and anxiety, although this relationship is less pronounced than that observed in people with schizophrenia. Future research involving larger clinical samples may provide more definitive insights into these associations.

The authors are willing to provide the complete statistical dataset upon request, together with supplementary material including scatterplots, histograms, and a detailed account of the pharmacotherapy administered to the patient group.

The research was conducted in accordance with the Declaration of Helsinki. The Jagiellonian University Bioethics Committee issued a favourable opinion on the project (approval nos. 1072.6120.252.2021 and 1072.178.2022).

REFERENCES

- Severance EG, Prandovszky E, Castiglione J, Yolken RH. Gastroenterology issues in schizophrenia: why the gut matters. *Curr Psychiatry Rep.* 2015;17(10):74. doi:10.1007/s11920-015-0574-0.
- Lu C, Jin D, Palmer N, Fox K, Kohane IS, Smoller JW, et al. Large-scale real-world data analysis identifies comorbidity patterns in schizophrenia. *Transl Psychiatry.* 2022;12(1):154. doi:10.1038/s41398-022-01916-y.
- Grant RK, Brindle WM, Donnelly MC, McConville PM, Stroud TG, Bandieri L, et al. Gastrointestinal and liver disease in patients with schizophrenia: A narrative review. *World J Gastroenterol.* 2022;28(38):5515-5529. doi:10.3748/wjg.v28.i38.5515.
- Severance EG, Yolken RH, Eaton WW. Autoimmune diseases, gastrointestinal disorders and the microbiome in schizophrenia: more than a gut feeling. *Schizophr Res.* 2016;176(1):23-35. doi:10.1016/j.schres.2014.06.027.
- Koizumi T, Uchida H, Suzuki T, Sakurai H, Tsunoda K, Nishimoto M, et al. Oversight of constipation in inpatients with schizophrenia: a cross-sectional study. *Gen Hosp Psychiatry.* 2013;35(6):649-652. doi:10.1016/j.genhosppsych.2013.06.007.
- Virtanen T, Eskelinen S, Sailas E, Suvisaari J. Dyspepsia and constipation in patients with schizophrenia spectrum disorders. *Nord J Psychiatry.* 2017;71(1):48-54. doi:10.1080/08039488.2016.1217044.
- Engels G, Francke AL, van Meijel B, Douma JG, de Kam H, Wesselink W, Houtjes W, Scherder EJ. Clinical pain in schizophrenia: a systematic review. *J Pain.* 2014;15(5):457-467. doi:10.1016/j.jpain.2013.11.005.
- Carrasco-Picazo JP, González-Teruel A, Gálvez-Llompart AM, Carbonell-Asins JA, Hernández-Viadel M. Pain sensitivity in patients with schizophrenia: a systematic review and meta-analysis. *Actas Esp Psiquiatr.* 2023;51(1):29-40.
- Gradius JL, Farkas DK, Svensson E, Ehrenstein V, Lash TL, Toft Sørensen H. Posttraumatic stress disorder and gastrointestinal disorders in the Danish population. *Epidemiology.* 2017;28(3):354-360. doi:10.1097/EDE.0000000000000622.
- Seow LSE, Ong C, Mahesh MV, Sagayadevan V, Shafie S, Chenga SA, Subramaniam M. A systematic review on comorbid post-traumatic stress disorder in schizophrenia. *Schizophr Res.* 2016;176(2-3):441-451. doi:10.1016/j.schres.2016.05.004.
- Seong A, Cho SE, Na KS. Prevalence and correlates of comorbid posttraumatic stress disorder in schizophrenia-spectrum disorder: A systematic review and meta-analysis. *Psychiatry Investig.* 2023;20(6):483-492. doi:10.30773/pi.2022.0353.
- Hartley S, Barrowclough C, Haddock G. Anxiety and depression in psychosis: a systematic review of associations with positive psychotic symptoms. *Acta Psychiatr Scand.* 2013;128(5):327-346. doi:10.1111/acps.12080.
- Kanchanatawan B, Thika S, Sirivichayakul S, Carvalho AF, Geffard M, Maes M. In schizophrenia, depression, anxiety, and psychosomatic symptoms are strongly related to psychotic symptoms and excitation, impairments in episodic memory, and increased production of neurotoxic tryptophan catabolites: a multivariate and machine learning study. *Neurotox Res.* 2018;33(3):641-655. doi:10.1007/s12640-018-9868-4.
- Bergmann N, Hahn E, Hahne I, Zierhut M, Ta TMT, Bajbouj M, Pijnenborg GHM, Böge K. The relationship between mindfulness, depression, anxiety, and quality of life in individuals with schizophrenia spectrum disorders. *Front Psychol.* 2021;12:708808. doi:10.3389/fpsyg.2021.708808.
- Walter SA, Jones MP, Talley NJ, Kjellström L, Nyhlin H, Andreasson AN, Agréus L. Abdominal pain is associated with anxiety and depression scores in a sample of the general adult population with no signs of organic gastrointestinal disease. *Neurogastroenterol Motil.* 2013;25(9):741-e576. doi:10.1111/nmo.12155.

16. Sperber AD, Bangdiwala SI, Drossman DA, Ghoshal UC, Simren M, Tack J, Whitehead WE, Dumitrascu DL, Fang X, Fukudo S, Kellow J, Okeke E, Quigley EMM, Schmulson M, Whorwell P, Archampong T, Adibi P, Andresen V, Benninga MA, Bonaz B, Palsson OS. Worldwide prevalence and burden of functional gastrointestinal disorders, results of Rome Foundation Global Study. *Gastroenterology*. 2021;160(1):99-114.e3. doi:10.1053/j.gastro.2020.04.014.
17. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Arlington: American Psychiatric Publishing; 2013. doi:10.1176/appi.books.9780890425596.
18. Kulich KR, Madisch A, Pacini F, Piqué JM, Regula J, Van Rensburg CJ, et al. Reliability and validity of the Gastrointestinal Symptom Rating Scale (GSRS) and Quality of Life in Reflux and Dyspepsia (QOLRAD) questionnaire in dyspepsia: a six-country study. *Health Qual Life Outcomes*. 2008;6:12. doi:10.1186/1477-7525-6-12.
19. Kulich KR, Regula J, Stasiewicz J, Jasiński B, Carlsson J, Wiklund I. Psychometric validation of the Polish translation of the Gastrointestinal Symptom Rating Scale (GSRS) and Quality of Life in Reflux and Dyspepsia (QOLRAD) Questionnaire in patients with reflux disease. *Pol Arch Med Wewn*. 2005;113(3):241-249.
20. Beck AT, Steer RA, Brown G. Beck Depression Inventory–II (BDI-II). APA PsycTests. 1996. doi:10.1037/t00742-000.
21. Spielberger CD, Gorsuch RL, Lushene R, Vagg PR, Jacobs GA. Manual for the State-Trait Anxiety Inventory. Palo Alto: Consulting Psychologists Press; 1983.
22. Cloitre M, Shevlin M, Brewin CR, Bisson JI, Roberts NP, Maercker A, Karatzias T, Hyland P. International Trauma Questionnaire (ITQ). APA PsycTests. 2018. doi:10.1037/t72132-000.
23. Nijenhuis ERS, Van der Hart O, Kruger K. The psychometric characteristics of the Traumatic Experiences Questionnaire (TEC): First findings among psychiatric outpatients. *Clin Psychol Psychother*. 2002;9(3):200-210. Transl. Pietkiewicz & Tomalski, 2016.
24. Endler NS, Parker JDA. The multidimensional assessment of coping: A critical evaluation. *J Pers Soc Psychol*. 1990;58(5):844-854. doi:10.1037/0022-3514.58.5.844.
25. Bernstein DP, Fink L, Handelsman L, Foote J. Childhood Trauma Questionnaire (CTQ). APA PsycTests. 1994. doi:10.1037/t02080-000.
26. Addington D, Addington J, Maticka-Tyndale E. Specificity of the Calgary Depression Scale for schizophrenics. *Schizophr Res*. 1994;11(3):239-244. doi:10.1016/0920-9964(94)90018-0.
27. Turek A, Śmierciak N, Szwajca M, Karcz P, Krzyściak W, Batko B, Magacz M, Donicz P, Furman K, Bryll A, Popiela T, Pilecki M. Serum LBP and zonulin levels with brain MRS findings and gastrointestinal symptoms in schizophrenia and health. *Brain Behav Immun Health*. 2026;53:101206. doi:10.1016/j.bbih.2026.101206.
28. Turek A, Śmierciak N, Szwajca M, Karcz P, Krzyściak W, Batko B, Donicz P, Furman K, Bryll A, Bystrowska B, Popiela T, Pilecki M. Associations between brain and blood metabolites with gastrointestinal discomfort in schizophrenia and healthy controls. *J Psychiatr Res*. 2026;201:15-28. doi:10.1016/j.jpsychires.2026.05.040.
29. Wickham H, RStudio. tidyverse: Easily Install and Load the “Tidyverse” (Version 2.0.0) [Computer software]. 2023.
30. Revelle W. psych: Procedures for Psychological, Psychometric, and Personality Research (Version 2.4.12) [Computer software]. 2024.
31. Wright K. pals: Color Palettes, Colormaps, and Tools to Evaluate Them (Version 1.10) [Computer software]. 2025.
32. Schloerke B, Cook D, Larmarange J, Briatte F, Marbach M, Thoen E, Elberg A, Toomet O, Crowley J, Hofmann H, Wickham H. GGally: Extension to “ggplot2” (Version 2.2.1) [Computer software]. 2024.
33. DeBattista C, Schatzberg AF. The Black Book of Psychotropic Dosing and Monitoring. *Psychopharmacol Bull*. 2024;54(2):83-117.
34. Every-Palmer S, Nowitz M, Stanley J, Grant E, Huthwaite M, Dunn H, Ellis PM. Clozapine-treated patients have marked gastrointestinal hypomotility, the probable basis of life-threatening gastrointestinal complications: a cross sectional study. *EBioMedicine*. 2016;5:125-134. doi:10.1016/j.ebiom.2016.02.020.
35. Maier L, Pruteanu M, Kuhn M, Zeller G, Telzerow A, Anderson EE, Brochado AR, Fernandez KC, Dose H, Mori H, Patil KR, Bork P, Typas A. Extensive impact of non-antibiotic drugs on human gut bacteria. *Nature*. 2018;555(7698):623-628. doi:10.1038/nature25979.
36. Dias MF, Nogueira YJA, Romano-Silva MA, Marques de Miranda D. Effects of antipsychotics on the gastrointestinal microbiota: a systematic review. *Psychiatry Res*. 2024;336:115914. doi:10.1016/j.psychres.2024.115914.
37. Kannampalli P, Sengupta JN. Role of principal ionotropic and metabotropic receptors in visceral pain. *J Neurogastroenterol Motil*. 2015;21(2):147-158. doi:10.5056/jnm15026.
38. Garcia-Leon MA, Fuentes-Claramonte P, Valiente-Gómez A, Natividad C, Salgado-Pineda P, Gomar JJ, Guerrero-Pedraza A, Portillo F, Ortiz-Gil J, Alonso-Lana S, Maristany T, Raduà J, Salvador R, Sarró S, Pomarol-Clotet E. Altered brain responses to specific negative emotions in schizophrenia. *Neuroimage Clin*. 2021;32:102894. doi:10.1016/j.nicl.2021.102894.
39. Trotti RL, Abdelmageed S, Parker DA, Sabatinelli D, Tamminga CA, Gershon ES, Keedy SK, Keshavan MS, Pearson GD, Sweeney JA, McDowell JE, Clementz BA. Neural processing of repeated emotional scenes in schizophrenia, schizoaffective disorder, and bipolar disorder. *Schizophr Bull*. 2021;47(5):1473-1481. doi:10.1093/schbul/sbab018.
40. Zhao M, Ma J, Wu Y, Zhang Y, Wang L, Song H, Sun X. Depressive and anxiety symptoms among schizophrenia

- patients. *J Affect Disord.* 2024;362:749-754. doi:10.1016/j.jad.2024.07.130.
41. Krynicki CR, Upthegrove R, Deakin JFW, Barnes TRE. The relationship between negative symptoms and depression in schizophrenia: a systematic review. *Acta Psychiatr Scand.* 2018;137(5):380-390. doi:10.1111/acps.12873.
 42. Defrin R, Schreiber S, Ginzburg K. Paradoxical pain perception in posttraumatic stress disorder: the unique role of anxiety and dissociation. *J Pain.* 2015;16(10):961-970. doi:10.1016/j.jpain.2015.06.010.
 43. Sakuma T, Muratsubaki T, Kano M, Kanazawa M, Fukudo S. Association between disturbance of self-organization and irritable bowel syndrome in Japanese population using the international trauma questionnaire. *Sci Rep.* 2024;14(1):18412. doi:10.1038/s41598-024-68196-y.
 44. Park SH, Videlock EJ, Shih W, Presson AP, Mayer EA, Chang L. Adverse childhood experiences are associated with irritable bowel syndrome and gastrointestinal symptom severity. *Neurogastroenterol Motil.* 2016;28(8):1252-1260. doi:10.1111/nmo.12826.
 45. Gnat L, Mihajlovic V, Jones K, Tripp DA. Differentiating childhood traumas in inflammatory bowel disease. *J Can Assoc Gastroenterol.* 2023;6(5):172-178. doi:10.1093/jcag/gwad026.
 46. Kurogi T, Yokoi K, Hayashi R, et al. Emotion-oriented coping styles are associated with higher stress response and lower quality of life in patients with schizophrenia. *Curr Psychol.* 2024;43(41):32993-33002. doi:10.1007/s12144-024-06857-x.
 47. Dickson H, Laurens KR, Cullen AE, Hodgins S. Academic achievement and schizophrenia: a systematic meta-analysis. *Psychol Med.* 2020;50(12):1949-1965. doi:10.1017/S0033291720002354.
 48. Holm M, Taipale H, Tanskanen A, Tiihonen J, Mittendorfer-Rutz E. Employment among people with schizophrenia or bipolar disorder: A population-based study using nationwide registers. *Acta Psychiatr Scand.* 2021;143(1):61-71. doi:10.1111/acps.13254.