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Lying to myself that I feel just fine makes my gut sick: gastrointestinal symptoms explained by experiential avoidance

Kad lažem samoj sebi da sam dobro činim loše svom trbuhu: gastrointestinalni simptomi objašnjeni izbjegavanjem doživljaja

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Summary

Objective: To analyze the correlation between sociodemographic variables, emotional states (anxiety, depression), emotion regulation strategies (experiential avoidance, emotion suppression) and acute gastrointestinal symptoms.

Method: On a convenience sample of 186 subjects, data on acute gastrointestinal symptoms, emotions (depression and anxiety), emotion regulation strategies (emotion supression and experiential avoidance) and sociodemographic variables have been gathered using a Physical health questionnaire (PHQ), Zung depression scale, State trait anxiety inventory (STAI), Emotion regulation questionnaire (ERQ) and Brief experiential avoidance questionnaire (BEAQ). Data was analyzed by multiple hierarchical regression. In the final model 32% of variance of acute gastrointestinal symptoms was explained, and statistically significant predictors were depression and experiential avoidance. Higher levels of depression and experiential avoidance were associated with more frequent acute gastrointestinal symptoms.

Conclusion: A high prevalence of clinically relevant symptoms of anxiety (63%) and depression (41%), as well as a positive correlation between emotion, emotion regulation strategies and acute gastrointestinal symptoms emphasize the importance of providing psychological support to patients with gastrointestinal system disorders. Independent contribution of experiential avoidance to the prediction of acute gastrointestinal symptoms shows that in order to understand the psychological aspect of gastrointestinal symptoms it is important to have insight not only into emotions, but also into the way they are being regulated.

Key words: acute gastrointestinal symptoms, anxiety, depression, experiential avoidance, emotion supression

Sažetak

Cilj: Analizirati povezanost između sociodemografskih varijabli, emocionalnih stanja (anksioznost, depresivnost), strategija regulacije emocija (izbjegavanje doživljaja, potiskivanje emocija) i akutnih probavnih simptoma

Metode: Na prigodnom uzorku od 186 sudionika pomoću Upitnika tjelesnog zdravlja (PHQ), Zungovog upitnika depresivnosti, Upitnika anksioznosti kao stanja i osobine ličnosti (STAI), Upitnika regulacije emocija (ERQ) i Kratkog upitnika izbjegavanja doživljaja (BEAQ), prikupljeni su podaci o akutnim probavnim simptomima, emocijama (depresivnosti i anksioznosti), strategijama regulacije emocija (potiskivanje emocija i izbjegavanje doživljaja) i sociodemografskim varijablama. Na podacima je primijenjena hijerarhijska regresijska analiza. U finalnom modelu objašnjeno je 32% varijance akutnih gastrointestinalnih simptoma, pri čemu su statistički značajni prediktori bili depresivnost i izbjegavanje doživljaja. Intenzivnija depresivnost i izraženija sklonost izbjegavanju doživljaja bili su povezani s učestalijim akutnim gastrointestinalnim simptomima.

Zaključak: Visoka zastupljenost klinički relevantnih simptoma anksioznosti (63%) i depresivnosti (41%), te pozitivna povezanost i emocija i strategija regulacije emocija s akutnim gastrointestinalnim simptomima, upućuje na važnost pružanja psihološke podrške bolesnicima s poremećajima gastrointestinalnog sustava. Nezavisan doprinos izbjegavanja doživljaja predikciji akutnih gastrointestinalnih simptoma pokazuje da je za razumijevanje psihološkog aspekta gastrointestinalnih simptoma važno imati uvid, ne samo u emocije, već i u način na koji ih se regulira.

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There is no pain you are receding
A distant ship smoke on the horizon
…
I have become comfortably numb
(Pink Floyd, „Comfortably numb“)

Introduction

Symptoms that can be attributed to digestive system dysfunction include abdominal pain, diarrhea, constipation, bloating, nausea, and vomiting. All of these symptoms may be caused by an organic (OGD) or functional gastrointestinal disorder (FGD). With OGDs (for example, gastrointestinal cancer, inflammatory bowel disease, celiac disease, ulcer disease and others) there is an accompanying structural abnormality of the gastrointestinal system that may explain the onset of digestive symptoms, while with FGDs, despite the symptoms present, it is not possible to establish an accompanying structural abnormality. According to the Rome IV classification, FGDs include 33 disorders of which the most common are irritable bowel syndrome, functional dyspepsia, and functional constipation, and they also include functional nausea and vomiting, functional diarrhea and others.[1,2] In the population of people between the ages of 20 and 40, the most common OGDs are inflammatory bowel diseases, including Crohn's disease and ulcerative colitis.[3] In a study conducted just before the outbreak of the COVID 19 pandemic (2018 and 2019) in 33 countries on 6 continents, the estimated prevalence of gastrointestinal disorders in the general population for FGDs is 40% and for OGDs approximately 8%.[4]

The digestive system has a complex intrinsic nervous system, the so-called enteric nervous system (ENS), also known as “the abdominal brain”. The total number of enteric neurons in humans is between 400 and 600 million, which is more than the total number of neurons in all sympathetic and parasympathetic ganglia combined and equal to the number of neurons in the spinal cord. The ENS contains more than 30 neurotransmitters, including neurotransmitters associated with psychopathological processes (serotonin, dopamine, alpha aminobutyric acid, acetylcholine).[5] Moreover, 95% of the total amount of serotonin[6,7] and 50% of dopamine[8] in the human body is found in the ENS. Furthermore, the ENS is closely related to the microbiome, i.e. about 100 trillion bacteria that are found in the intestines and play an important role in the immune system, brain function and signaling systems within the central nervous system (CNS).[9] The “highest” level of regulation of the gastrointestinal system is corticolimbic regulation, i.e. regulation from the centers in the CNS that regulate the work of the autonomic nervous system (ANS),[10] as well as numerous psychological and behavioral processes, including the hypothalamus, amygdala, and prefrontal cortex. The gastrointestinal tract is innervated only by parasympathetic, and not sympathetic fibers.[11] Recent research suggests that there is a two-way relationship between the CNS and ENS.[9] For example, probiotic treatment is effective in relieving anxiety, depression, and experience of stress.[12] Also the other way around, antidepressants are effective in treating FGDs.[13] Recognition of the connection between psychological and gastrointestinal status and the mediating role that the nervous system plays in the interaction between psychological processes and the digestive system has led to the use of the terms psychogastroenterology[14] and psychoneurogastroenterology[15] in scientific literature.

The biopsychosocial model of the pathogenesis of gastrointestinal disorders includes predisposing biological/physiological, psychological and social/environmental factors.[16] In the case of FGDs, the predisposing biological factors are genetic predisposition, female gender, immune system dysfunction, hypothalamic-pituitary-adrenal axis dysfunction, digestive infection or inflammation, and disrupted microbiome structure. Psychological factors that often precede or exacerbate FGD symptoms are anxiety, depression, panic, post-traumatic stress disorder and somatization disorders. Predisposing social/environmental factors are emotional, physical and sexual abuse in childhood, stressful life events in adulthood (e.g. divorce, grief), lack of social support, and others.[17-19] The application of the biopsychosocial model in OGDs research is less frequent than in the case of FGDs, but there are still studies that suggest the importance of psychological and social factors in the etiology of OGDs[20-24] as well.

When it comes to age, gender, income and education as predictors of acute gastrointestinal symptoms (AGS), the numerous findings so far are consistent only in the case of age, while the relationship between gender, income, education and AGS is complex, dependent on interaction with other variables, and the results of different studies are contradictory. When it comes to age, the results of various studies consistently suggest that acute gastrointestinal symptoms are in negative correlation

with age.[25-29] Regarding gender, some of the research to date shows that female gender is predictive for AGS,[4,25,26,29] while others suggest an interaction between gender and age in the way that in the younger population gastrointestinal symptoms are more common in men and vice versa.[27] The relationship between acute gastrointestinal symptoms and income is complex and it is in interaction with other sociodemographic variables: gastrointestinal symptoms may be more common in people with higher incomes,[27] equally common in men with different income levels and more common in women with lower incomes than in women with higher incomes,[26] more common in those with the lowest and highest incomes, but only in the case of lower educational status, i.e. equally common in people of different income levels if they are highly educated,[25] in a negative correlation with income on the periphery and in zero correlation with income in the city center[30] etc. Findings on the relationship between educational status and AGS are very heterogeneous: in some cases the frequency of AGS decreases with the increase in educational status,[29] in other cases it increases,[25,30] and there are also studies that have found that education and AGS are unrelated.[26]

When it comes to psychological or emotional factors that contribute to gastrointestinal symptoms and disorders, it is important to distinguish between emotions (e.g. anxiety, depression) and the way a person manages his/her emotions, i.e. emotion regulation. Emotion consists of three parts: (1) subjective/mental experience (feeling), (2) motor expression, and (3) physiological arousal. Subjective experience/feeling is "internal" information (it provides information about the quality of the emotion to the person experiencing it), and motor expression, as well as externally observable effects of physiological arousal, are "external" information – they provide information about the quality of emotion to a person's social environment.

Emotion regulation refers to the implementation of a goal to begin, stop, or otherwise modulate the trajectory of an emotion[31] and it involves a wide range of reactions, including efforts to begin, delay, complete, or modify the form and/or content, or modulate the quality and/or quantity of thoughts, emotions, behaviors, or physiological reactions.[32] Therefore, emotion regulation can be viewed as a change in the emotion trajectory that would take place in the absence of an emotion regulation strategy. One possible division of the many strategies of emotion regulation is that of adaptive and non-adaptive, or those associated with lower or with higher levels of psychopathological symptoms. Some of the adaptive strategies are acceptance, cognitive restructuring, and expression of emotions. On the other hand, emotion suppression, denial, and avoidance are some examples of non-adaptive strategies and can therefore be defined not as regulation but as dysregulation of emotions.[33] In a meta-analysis by Schaefer et al.[34] adaptive emotion regulation strategies (cognitive restructuring, problem solving, and acceptance) were negatively correlated with depression and anxiety, while non-adaptive strategies (avoidance, supression and rumination) were positively correlated with depression and anxiety. In addition to psychopathological symptoms, emotion dysregulation is positively correlated with childhood abuse.[35]

Recent studies suggest that emotion dysregulation is also associated with bodily symptoms: elevated levels of inflammatory markers – C-reactive protein,[36] IL-17 A, IL-2, IL-6, TNF-α and interferon-γ,[37] reduced volume of gray matter in the amygdala,[38] decreased heart rate variability,[39,40] sleep disorders in people with generalized anxiety disorder,[41] greater risk factors for cardiovascular disease[42] and a higher intensity of physical symptoms in individuals with borderline personality disorder,[43] adults abused in childhood[44] and those with asthma.[45] On the other hand, adaptive strategies of emotion regulation are not associated with the severity of bodily symptoms[45] and with the levels of inflammatory markers,[37] and a greater propensity to use adaptive emotion regulation strategies is positively correlated with physical health.[38] Comparing healthy and asthmatic patients, healthy people are more prone to adaptive and those with asthma to non-adaptive emotional regulation strategies.[45]

Emotion dysregulation is positively correlated with alexithymia, the inability to recognize and express emotions.[46-49] Alexithymia, in turn, is associated with decreased heart rate variability,[50] peptic ulcer, irritable bowel syndrome, inflammatory bowel disease, asthma, diabetes, heart disease, malignant diseases and progression of tumor invasion, physical pain, dermatological disorders[45,51-54] and multiple sclerosis[55] as well as mortality in men but not in women.[56]

Two common and frequently used strategies for emotion (dys)regulation are the supression of the expression of emotions, i.e. refraining from *behaviour* that expresses emotions[57] as well as experiential avoidance, which means efforts aimed at inhibiting *feelings*, i.e. the experience of emotion.[58] Both emotion supression and experiential avoidance are negatively correlated with measures of both psychological[59,60] and physical health,[61,62] however, it seems that experiential avoidance is a more severe form of emotion dysregulation. For example, the correlation between experiential avoidance and anxiety is about 0.60,[63-65]

while the correlation between emotion supression and anxiety is substantially lower and amounts to about 0.20.[57,66-70] It can be speculated that experiential avoidance is a more pathological form of emotion dysregulation because when suppressing emotions a person tries to modulate the motor and physiological expression of an emotion, but the feeling of that emotion can still remain, while in the case of experiential avoidance the person supresses the motor expression, the physiological expression, and also the feeling itself, which are all three components of the total three components of emotion. In other words, in emotion supression the experienced emotion is hidden only "outwards", i.e. the person is trying to hide it from others, while in experiential avoidance the person is hiding the emotion primarily in relation to oneself.

Emotion (dys)regulation strategies are probably, for the most part, adopted during childhood. Children learn how to regulate emotions in three ways: by observation, through specific parental instructions and behaviors (emotion socialization) and through the emotional climate in the family (attachment style, child rearing style, emotional expressiveness of family members, quality of the relationship of parents).[71] Speaking of emotion socialization, if there is continuous information from the social environment about certain feelings being undesirable (injunctions), it can be speculated that the child will adjust in such a way that at first they will not show unacceptable feelings to others (emotion supression) and that it is possible that over time they themselves will also dissociate from experiencing the undesirable feelings (experiential avoidance). It is often the case that some emotions are almost universally considered unacceptable: e.g. sadness, especially the expression of sadness by crying in men. Consequently, the injunction against crying for male children is (almost) universally considered a common, desirable, "normal", even – necessary part of "upbringing". It can be assumed that the basic goal of suppressing the expression of emotions is of a social nature, i.e. that the goal is not to show emotion to others, and furthermore that underlying that goal is a desire to avoid social rejection. When it comes to experiential avoidance, the goal of this strategy is probably both not to show emotion to others and reduce your own intensity of negative affect.

With the aim of further clarifying the relationship between emotions and the strategy of their regulation in the context of the biopsychosocial model of gastrointestinal disorders, this paper will analyze the contribution of sociodemographic variables (age, gender, socioeconomic status), emotions (anxiety, depression) and emotion regulation (emotion supression, experiential avoidance) to the frequency of acute digestive symptoms (constipation, diarrhea, nausea, indigestion) in the past month.

Method

Participants and procedure

A convenience sample was used that consisted of 200 US smartphone users who completed the questionnaires on their smartphones via the Pollfish platform in the first half of 2021. 14 participants did not answer the question on personal income and therefore the total statistical analysis was conducted on a subsample of 186 participants. The share of women was 52% (n=104). The average age of the participants was 43 years (M=43.5, sd=1.05). The distribution of participants with regard to education and personal income is shown in Table 1.

Table 1 Education and yearly income (n=186)
Tablica 1. Obrazovanje i godišnji osobni prihodi (n=186)

		n	%
Education *Obrazovanje*	middle school / *osnovna škola*	1	0,5
	high school / *srednja škola*	42	22,6
	vocational technical college / *viša strukovna škola*	19	10,2
	university / *fakultet*	62	33,3
	postgraduate / *postdiplomski studij*	62	33,3
Average yearly income in USD *Godišnji osobni prihod u američkim dolarima*	less than 25,000 / *manje od*	31	16,7
	25,000 - 49,999	36	19,4
	50,000 - 74,999	29	15,6
	75,000 - 99,999	25	13,4
	100,000 - 124,999	22	11,8
	125,000 - 149,999	13	7,0
	150,000 and more */ i više*	30	16,1

Instruments

Physical health questionnaire (Schat, Kelloway and Desmarais, 2005)[72] is a questionnaire consisting of 15 items distributed in 4 subscales: insomnia (4 items), headache (3 items), digestive system disorders (constipation, diarrhea, nausea, upset stomach) (4 items) and respiratory infections (3 items). The questionnaire was administered in such a way that the subjects stated how often they experienced symptoms listed in the questionnaire in the past month or how long the symptoms lasted during the same period.

There are 4 scores per subject in the questionnaire, one for each subscale. A higher score on the subscale indicates a higher frequency and/or longer duration of symptoms. In the case of the digestive disorders subscale, a higher score on the subscale indicates a higher incidence of AGS. The theoretical range from minimum to maximum score on the subscale is respectively 3 – 21 (headache and respiratory infections subscales), and 4 – 28 (insomnia and digestive system disorders subscales).

Zung depression scale (Zung, 1986)[73] is a questionnaire consisting of 20 items intended to measure depression. The subject gets 1 total score on the questionnaire. A higher score on the questionnaire indicates a more intense experience of depression. The theoretical range from minimum to maximum score on the questionnaire is 20 – 80. The cut-off score for diagnosing clinically significant symptoms of depression is 50.[74]

State-trait anxiety inventory, Form Y (Spielberger, Vag, Barker, Donham and Westberrry, 1980)[75] is a questionnaire consisting of 40 items distributed in 2 subscales: anxiety as a state (20 items) and anxiety as a trait (20 items). In this study, only the state anxiety subscale was applied. The subject gets one total score on the subscale. A higher score on the subscale indicates a more intense experience of state anxiety. The theoretical range from minimum to maximum score on the subscale is 20 – 80. The cut-off score for diagnosing clinically significant anxiety symptoms is 40.[76]

Emotion regulation questionnaire (Gross and John, 2003)[57] is a questionnaire of 10 items distributed in 2 subscales: cognitive restructuring (6 items) and emotion supression (4 items). The subject gets 2 scores on the questionnaire, one for each subscale. A higher score on the subscale indicates a greater tendency to regulate emotions through cognitive restructuring, or emotion supression. The theoretical range from minimum to maximum score on the subscale is 6 – 42 (cognitive restructuring subscale), or 4 – 28 (emotion supression subscale).

Brief experiential avoidance questionnaire (Gamez, Chmielewski, Kotov, Ruggero, Suzuki and Watson, 2014)[58] is a 15-item questionnaire designed to measure the propensity to regulate emotions using an experiential avoidance strategy. The subject gets 1 total score on the questionnaire. A higher score on the questionnaire indicates a greater propensity to regulate emotions by practicing experiential avoidance. The theoretical range from minimum to maximum score on the questionnaire is 15 – 90.

Data on gender, age, level of education and annual personal income (in US dollars) was also collected.

Statistical analysis

The data was analyzed in the SPSS (Statistical Package for Social Sciences), version 25. Descriptive statistical analysis was performed on all variables. To examine the contribution of sociodemographic variables, depression, anxiety, emotion suppression, and experiential avoidance to acute digestive symptoms, a hierarchical regression analysis was performed. Before conducting the regression analysis, the correlations between the predictors and the criteria were examined (Table 5).

Results

Descriptive statistics for the measure of physical health and measures of psychological status

Table 2 shows the arithmetic means, standard deviations, and reliability (Cronbach's alpha) for measures of physical health, anxiety, depression, emotion suppression, and experiential avoidance. All scales showed satisfactory reliability ($\alpha>=0.750$). Table 3 shows the percentage of participants who have clinically significant symptoms of depression or anxiety. 41% of participants had clinically significant symptoms of depression and 63% of participants had clinically significant symptoms of anxiety. Table 4 shows the percentage of participants who experienced AGS in the past month: 88% reported indigestion, 82% nausea, and 85% constipation or diarrhea.

Prediction of acute digestive symptoms

As can be seen from Table 5, levels of AGS in the subjects over the past month (constipation, diarrhea, nausea, indigestion) are statistically significantly positively correlated with annual personal income, anxiety, depression, emotion supression and experiential avoidance, and statistically significantly negatively correlated with age.

Table 2 Descriptive statistics for measures of acute gastrointestinal symptoms, depression, anxiety, emotion supression and experiential avoidance (n=186)
Tablica 2. Deskriptivna statistika za mjere akutnih probavnih simptoma, depresivnosti, anksioznosti, potiskivanja emocija i izbjegavanja doživljaja (n=186)

	M	sd	Reliability *Pouzdanost*
PHQ, subscale acute gastrointestinal symptoms *Upitnik tjelesnog zdravlja, podljestvica akutni probavni simptomi*	13,3	6,50	0,903
Zung depression scale *Zungov upitnik depresivnosti*	45,0	9,29	0,750
STAI, subscale state anxiety *Upitnik anksioznosti kao stanja i osobine ličnosti, podljestvica anksioznost kao stanje*	43,0	12,61	0,906
ERQ, subscale emotion suppression *Upitnik regulacije emocija, podljestvica potiskivanje emocija*	17,6	5,97	0,804
BEAQ *Kratki upitnik izbjegavanja doživljaja*	55,5	14,82	0,899

Table 3 Share of subjects with clinically significant symptoms of depression and anxiety (n=186)
Tablica 3. Udio sudionika s klinički značajnim simptomima depresivnosti i anksioznosti (n=186)

	%	n
Zung depression scale, score >=50 *Zungov upitnik depresivnosti, rezultat >=50*	41	77
STAI, subscale state anxiety, score >=40 *Upitnik anksioznosti kao stanja i osobine ličnosti, podljestvica anksioznost kao stanje, rezultat >=40*	63	117

Table 4 Share of subjects with acute gastrointestinal symptoms in the past month (n=186)
Tablica 4. Udio sudionika koji su u posljednjih mjesec dana doživjeli akutne gastrointestinalne simptome (n=186)

	%	n
Upset stomach / *Probavne smetnje*	88	163
Nausea / *Mučnina*	82	152
Constipation or diarrhea / *Zatvor ili dijareja*	85	158

Regarding the statistically significant correlation with gender, the variable "gender" was coded so that a positive correlation indicates that men have a higher score on the variable with which gender is correlated. In the case of AGS, men experienced AGS more often than women. Psychological variables are in higher correlations with AGS than sociodemographic ones, and in the highest correlation with AGS is experiential avoidance (r=0.45). Anxiety and depression (r=0.78) as well as emotion supression and experiential avoidance (r=0.67) are in high positive correlations with each other.

Experiential avoidance is numerically more highly correlated with both anxiety and depression and also with AGS than it is the case with emotion suppression, but the differences between the pairs of correlations experiential avoidance – emotion supression on a sample of the size used in this study (n=186) are statistically insignificant (correlations with anxiety: $r_{\text{emotion supression}}=0.23$; $r_{\text{experiential avoidance}}=0.31$; $z_{\Delta}=1.44$, $p_{\Delta}=0.075$; correlations with depression $r_{\text{emotion supression}}=0.29$; $r_{\text{experiential avoidance}}=0.35$; $z_{\Delta}=1.04$, $p_{\Delta}=0.148$; correlations with AGS $r_{\text{emotion supression}}=0.37$; $r_{\text{experiential avoidance}}=0.45$; $z_{\Delta}=1.16$, $p_{\Delta}=0.124$).

Table 5 Inter-correlations of measures of acute gastrointestinal symptoms, depression, anxiety, emotion supression and experiential avoidance (n=186)
Tablica 5. Korelacije između mjera akutnih probavnih simptoma, depresivnosti, anksioznosti, potiskivanja emocija i izbjegavanja doživljaja (n=186)

	v1	v2	v3	v4	v5	v6	v7	v8
Gastrointestinal symptoms (v1) *Probavni simptomi*								
Gender (v2) *Spol*	,13*							
Age (v3) Dob	-,22**	0,07						
Income (v4) *Prihod*	,29**	,27**	-0,08					
Education (v5) *Obrazovanje*	0,11	,21**	-0,04	,60**				
Depression (v6) *Depresivnost*	,39**	0,11	-,28**	0,09	-0,07			
Anxiety (v7) *Anksioznost*	,30**	0,12	-,30**	0,10	-0,01	,78**		
Emotion supression (v8) *Potiskivanje emocija*	,37**	,25**	-0,05	,28**	0,04	,29**	,23**	
Experiential avoidance (v9) *Izbjegavanje doživljaja*	,45**	,19**	-0,12	,25**	0,04	,35**	,31**	,67**

*p < 0 .05 ** p < 0.01

Gastrointestinal symptoms/*Probavni simptomi:* Physical health questionnaire (PHQ), subscale acute gastrointestinal symptoms/*Upitnik tjelesnog zdravlja, podljestvica akutni probavni simptomi*

Depression/*Depresivnost:* Zung depression scale/*Zungov upitnik depresivnosti*

Anxiety/*Anksioznost*: State trait anxiety inventory (STAI), subscale state anxiety/*Upitnik anksioznosti kao stanja i osobine ličnosti, podljestvica anksioznost kao stanje*

Emotion suppression/*Potiskivanje emocija:* Emotion regulation questionnaire (ERQ), subscale emotion suppression/*Upitnik regulacije emocija, podljestvica potiskivanje emocija*

Experiential avoidance/*Izbjegavanje doživljaja:* Brief experiential avoidance questionnaire (BEAQ)/*Kratki upitnik izbjegavanja doživljaja*

In the multiple hierarchical regression analysis (Table 6), sociodemographic variables were entered in the first step and they explained 13% of the variance, with lower age and higher income being statistically significant predictors of more frequent AGS. Anxiety and depression were added in the second step and in this step an additional 10% variance was explained. Statistically significant predictors of more frequent acute digestive symptoms were higher depression and higher income. Age in this step was no longer a statistically significant predictor. When it comes to anxiety, a probable reason for the lack of statistical significance of anxiety as a predictor is the high correlation of anxiety with depression. In the third and final step, variables related to emotion regulation were added – emotion supression and experiential avoidance. These variables explained an additional 8% of the variance. In this, the final model, statistically significant predictors were higher depression and more pronounced experiential avoidance, and a total of 32% of the variance was explained. Emotion supression probably did not prove to be a statistically significant predictor of AGS because of its association with experiential avoidance.

Table 6 Results of multiple hierarchical regression analysis with socio-demographic and psychological variables as predictors and acute gastrointestinal symptoms as criterion (n=186)
Tablica 6. Rezultati višestruke hijerarhijske regresijske analize sa sociodemografskim i psihološkim varijablama kao prediktorima i akutnim probavnim simptomima kao kriterijem (n=186)

Step *Korak*	Prediktori *Predictors*	β	R^2	Δ R^2
1	Gender/*Spol*	0,09	0,13	
	Age/*Dob*	-0,20**		
	Income/*Prihod*	0,31**		
	Education/*Obrazovanje*	-0,10		
	F(4,181)=6,953**			
2	Gender/*Spol*	0,05	0,23	0,10
	Age/*Dob*	-0,11		
	Income/*Prihod*	0,26**		
	Education/*Obrazovanje*	-0,04		
	Depression/*Depresivnost*	0,38**		
	Anxiety/*Anksioznost*	-0,06		
	F(6,179)=9,022**			
3	Gender/*Spol*	0,01	0,32	0,08
	Age/*Dob*	-0,11		
	Income/*Prihod*	0,16		
	Education/*Obrazovanje*	0,01		
	Depression/*Depresivnost*	0,29**		
	Anxiety/*Anksioznost*	-0,07		
	Emotion suppression/*Potiskivanje emocija*	0,11		
	Experiential avoidance/*Izbjegavanje doživljaja*	0,25**		
	F(8,177)=10,220**			

Discussion

(Dys)function of the gastrointestinal system, emotions and emotion (dys)regulation

Numerous studies suggest that there is an association between anxiety, depression and gastrointestinal disorders, both in the case of FGDs[77-79] and OGDs.[21,80-82] Especially in the case of FGDs, i.e. disorders of the gastrointestinal system in the absence of observable accompanying structural abnormalities, the question of the role of psychological factors arises. In this study on a convenience sample of participants from the United States it was found that 41% of participants had clinically relevant symptoms of depression and 63% had clinically relevant symptoms of anxiety. Comparison of these results in relation to the results that could be expected in the general population in the United States based on Zung depression scale[73] and State-trait anxiety inventory[75] is not possible, because recent or relevant norms for the general population are not available for the mentioned questionnaires. It is important to note that data for this study was collected during the coronavirus pandemic and that the same pandemic undoubtedly contributed to the rise in both anxiety and depression: fear of coronavirus has been associated with an increase in depression;[83] an increase in time spent following the news on coronavirus is a predictor of increase in anxiety and depression;[84] assessment of coronavirus-related risks is positively correlated with negative affect and negatively correlated with positive affect[85] etc. The increase in depression and anxiety after the onset of the pandemic is also visible from data collected in studies on the general population of the United States by NHIS and Household Pulse Survey: in the period from April to July 2019, the prevalence of anxiety and depressive disorders was estimated at 8.1% and 6.5%, respectively,[86] and in the period from 3 to 15 March 2021 at 31.3% and 26.2%.[87] In these studies, the PHQ-2 questionnaire (Patient Health Questionnaire) was used as a diagnostic tool for

depression, and the GAD-2 questionnaire (Generalized Anxiety Disorder Scale) was used for anxiety. In a meta-analysis by Luo et al., the average prevalence of anxiety and depression in 17 different countries from Asia, Europe, the Middle East, and Latin America between November 2019 and May 2020 was 33% and 28%, respectively.[88] There is a similarity between the results of this study and the findings of the NHIS and Household Pulse Survey in that clinically relevant symptoms of anxiety are more common than clinically relevant symptoms of depression, but the prevalence of both types of symptoms in this study is about twice that of anxiety and depression disorders in cited studies in an identical period on the general population in the United States.. One possible explanation for this discrepancy is that stricter criteria were used in the studies by other authors for both depression and anxiety. Overall, it can be concluded that the prevalence of clinically relevant symptoms of both anxiety and depression in this study is high and that this can be attributed in part to factors associated with the COVID-19 pandemic.

Psychological factors such as anxiety, depression, panic disorder, stress, post-traumatic stress disorder and somatization disorders often precede gastro-intestinal disorders. For example, elevated anxiety is a predictor of a newly diagnosed FGD 12 years later[77] and is associated with an increased risk of diagnosing functional dyspepsia over the next 10 years.[89] Women with a FGD were more likely to have a history of abuse in childhood than women without FGD.[90] Subjects with inflammatory bowel disease reported more stressful life events in general, more stressful life events before the age of 16, more traumatic stress, and more interpersonal violence than subjects in the control group.[91] Furthermore, psychological factors exacerbate the symptoms of pre-existing gastrointestinal disorders. For example, there was an increase in peptic ulcers following disasters – bombing of London,[92] economic collapse in Bulgaria,[93] earthquake in Kyoto[94] etc. Depression and anxiety are positively correlated with the recurrence rate of inflammatory bowel disease in the next 18 months.[95] Finally, gastrointestinal disorders may contribute to an increase in the intensity of psychopathological symptoms. Among subjects who did not have elevated levels of anxiety and depression at the start of the study, after 12 years those with FGD had a statistically significantly higher level of anxiety and depression than those without FGD.[77] Compared with inactive inflammatory bowel disease, active inflammatory bowel disease is associated with an increased risk for the presence of clinically relevant anxiety symptoms after two years.[81] These results, first of all, illustrate that psychological factors may have and probably do have a role in both the etiology and maintenance of gastrointestinal diseases. And secondly, it is evident that the relationship between gastrointestinal symptoms and disorders is two-way: psychological factors contribute to the worsening (or improvement!) of the symptoms of gastrointestinal disorders, and gastrointestinal disorders also affect psychological health.

This study found that more than 80% of participants experienced AGS: 88% reported indigestion, 82% nausea and 85% constipation or diarrhea in the past month. Compared to the estimate of the prevalence of FGDs of 40% and OGDs of 8% in a study by Sperber et al.,[4] the prevalence of AGS in this study is almost twice as high. Given that the study by Sperber et al. was conducted prior to the COVID-19 pandemic, that both anxiety and depression are correlates of AGS,[21,77-82] and that there has been a substantial increase in anxiety and depression after the pandemic,[87,88] it is quite possible that a very high prevalence of AGS in participants in this study is associated with an increase in anxiety and depression after the pandemic outbreak.

It is only recently that studies have tackled the role of not only emotions themselves, but also the role of the way a person *regulates* emotions, in gastro-intestinal and other bodily disorders. The few studies on emotion regulation styles in patients with gastrointestinal symptoms and/or disorders suggest that these symptoms and disorders are associated with emotion regulation strategies that increase overall stress levels.[61,96-99] Numerous studies on the relationship between emotion supression and physical health suggest that emotion supression is associated with increased cortisol activation[100] and that it may contribute to the development of cardiovascular disease[101,102] and shorten overall life expectancy.[62] Research on the relationship between emotion supression and gastrointestinal system status has not been identified. When it comes to experiential avoidance, it is positively correlated with irritable bowel symptoms,[98] abdominal pain and bloating[99] and generally with a number of acute bodily symptoms.[61]

When speaking of the relationship between emotions, emotion regulation and digestive or any other bodily disorders, the question is whether the development of a physical disorder is due to the fact that the person has experienced an emotion in any way or due to the way in which the person "processes", or regulates, the experienced emotion. Emotions that are traditionally perceived as "negative" (e.g. anger, fear, sadness) are a completely natural and expected reaction to a certain set of circumstances (e.g. grief at the experience of loss). In some cases, the pathological process or condition is indicated by the *absence* of an

expected emotional response – for example, the absence of fear and anger in everyday situations may indicate damage of the amygdala.[103] When it comes to anxiety and depression, determining the boundary between a normal and a pathological reaction can be very complex.[104] Regardless of where this boundary is located in an absolute sense, there is no doubt that in a relative sense the aforementioned boundary is closer to lower and farther than higher intensity of anxiety and depression symptoms. Experiential avoidance reduces anxiety and depression in the short term, while in the long run and somewhat paradoxically – it contributes to their increase.[105-107] Emotion supression also contributes to an increase in anxiety in the long run, while in relation to depression the results of existing research are contradictory.[107,108] On the other hand, adaptive emotion regulation strategies are negatively correlated with depression and anxiety.[34] Therefore, in interpreting the findings on the relationship between anxiety, depression, and gastrointestinal symptoms and disorders the question arises to which extent the measured anxiety and depression are caused by their dysregulation.

The link between emotions and their regulation on the one hand and gastrointestinal symptoms and disorders on the other is the nervous system – ENS, (the rest of) ANS, CNS and microbiome. Signals from the microbiome to the brain appear to be transmitted by multiple mechanisms, including endocrine and neurocrine pathways, while on the other hand the brain can modify the composition and activity of the microbiome. There are indications that the microbiome affects brain functions associated with amygdala function (social behavior, emotion regulation, stress and pain modulation systems) and the neurotransmitter systems of the brain. The microbiome also appears to be necessary for the normal development of the amygdala.[109,110] People with more gray matter in the amygdala are better at regulating their emotions and are physically healthier.[38] Emotion supression is faster in reducing the intensity of "negative" emotion measured through evoked potentials,[111] but a greater tendency to suppress emotions is also associated with less efficient information processing in multiple brain networks[112] and with a smaller mass of the ventromedial prefrontal cortex.[113] Decreased volume of the left insula, left amygdala, orbital frontal cortex, and striatum are structural correlates of alexithymia.[114] The paracentral lobule, a part of the primary motor cortex involved in the regulation of bladder and bowel emptying, is more associated with other brain nodes in its cortical network in people with more pronounced alexithymia.[115] Given the above results, i.e. that it is possible that dysregulation of emotions leads to negative changes in the function and structure of the brain, and the previously cited findings that emotion dysregulation is also associated with FGDs, it can be speculated that, in FGDs, accompanying structural abnormalities in the gastrointestinal system may not be found, but that they could be found in the brain / nervous system. The parasympathetic system is regulated from the centers in the CNS, including the amygdala and prefrontal cortex.[10] If parasympathetic activity in the lower gastrointestinal tract is excessive, it leads to diarrhea, and if it is insufficient, it can be associated with constipation.[11] It is also possible that nervous system abnormalities are antecedents of both FGDs and OGDs. ANS imbalance is a correlate of many physical diseases and symptoms, including gastrointestinal, but is initially asymptomatic.[11]

Prediction of the frequency of acute gastrointestinal symptoms

The results of this study show that emotion regulation, specifically experiential avoidance, explains the additional variance of AGS (diarrhea, constipation, nausea, indigestion) in the previous month on top of the variance explained by emotional status, i.e. depression and personal income. These results are consistent with previous findings of a negative correlation between digestive symptoms and depression[21,77-82] as well as digestive symptoms and experiential avoidance.[98,99] Although in the first and second steps of the regression analysis age and income represented statistically significant predictors of AGS, in the final model they lost their statistical significance, probably due to the negative correlation of age with depression and the positive correlation of income with experiential avoidance. This finding suggests that depression and experiential avoidance could be mediators in explaining the relationship of age and income with AGS. First, when it comes to age and AGS, a lower incidence of AGS in the elderly is a completely expected finding.[25-29] With regard to age and depression, the incidence of depressive symptoms appears to decrease with age.[116,117] When it comes to income and incidence of AGS, the findings of other authors are very heterogeneous[25-27,30] and some of them[27] are consistent with the results obtained in this study. Given the high correlation between income and education (r=0.60, Table 5) it is possible that participants with higher incomes simply notice AGS more. Regarding income and experiential avoidance, no studies have been identified that directly analyze the relationship between the two variables. Kashdan i Breen[118] found that experiential avoidance mediates the relationship between materialistic values on the one

hand and elevated "negative" emotions, a reduced sense of meaning in life and less gratitude on the other. The authors speculate that materialistic values collide with the acceptance of oneself in general and thus with the acceptance of one's own emotions and experiences. It is possible that participants with higher incomes in this research have more pronounced materialistic values and that they accept themselves less. Given the low correlation of gender and zero correlation of education with AGS in this study and given the contradictory findings of other authors on the relationship of gender[4,25-27,29] and education,[26,29,30] with AGS, the lack of predictiveness for gender and education for the frequency of AGS is not unexpected.

In the second step of the regression analysis, another statistically significant predictor, in addition to income, was depression. On the other hand, despite its statistically significant correlation with AGS, anxiety was not a significant predictor, probably due to its high correlation with depression. In the third and final step, emotion regulation strategies are added, i.e. emotion supression and experiential avoidance. In this step, depression was still a statistically significant predictor, income lost its significance, and experiential avoidance proved to be an additional significant predictor. Emotion suppression, otherwise positively correlated with AGS, probably did not prove to be a statistically significant predictor of AGS due to its high correlation with experiential avoidance. The predictiveness of depression and experiential avoidance in relation to the incidence of AGS is in line with the findings of other authors.[21,77-82,98,99] The fact that experiential avoidance explains the independent and quantitatively very similar amount of AGS variance as does depression suggests that experiential avoidance, i.e. the way a person regulates their emotions contributes to the (dys)function of the gastrointestinal system regardless of the emotion itself that the person is experiencing. In addition, given the findings showing that experiential avoidance increases the intensity of depression in the long run[105-107] it can be speculated that experiential avoidance at least partially explains the part of variance attributed to depression in this study as well.

Conclusion

This study is one of the few studies that attempts to explain the variance of AGS through both measures of emotion (anxiety, depression) and measures of emotion dysregulation (emotion supression, experiential avoidance). The high prevalence of anxiety and depression in this sample and the positive correlation between anxiety, depression, emotion supression and experiential avoidance on the one hand and AGS on the other indicate the importance of paying attention to psychological and not only physical symptoms in the treatment of gastrointestinal disorders. The finding of this research, that dysregulation of emotions (experiential avoidance) explains an independent part of the AGS variance in addition to the part explained by the emotions themselves (depression), combined with a fairly reasonable assumption that at least part of the AGS variance explained by depression can actually also be attributed to experiential avoidance, suggest that it is possible that in order to understand the role of psychological factors both in the etiology and in the mechanisms of maintenance of gastrointestinal disorders emotional (dys)regulation is more important than the emotions themselves. If, as the findings of other authors show, adaptive strategies for regulating emotions are related to physical health, this indicates that emotions, whatever they may be, can be experienced in a way that does not harm the body. It is possible that such cultures in which most children receive a consistent message from their parents as well as from the wider social environment that all emotions are acceptable, necessary and important, i.e. cultures in which, as a rule, at least for certain emotions, children are not conveyed a more or less explicit message that they should be hidden, concealed, suppressed, eradicated, etc. („Boys don't cry!“, „Come on, you're not scared!“) are scarce or even non-existent. Given the growing number of findings showing that this way of dealing with one's own emotions is detrimental to one's health in the long run, it seems that it would be useful to define such "educational" practices as unfavorable for the emotional development of children and to design public health campaigns and other activities whose basic goal would be to promote adaptive strategies for the regulation of emotions in the general population. Such activities would very likely contribute to the prevention and reduction of the incidence of not only gastrointestinal, but also many other physical and psychological disorders.

List of abbreviations
AGS – acute gastrointestinal symptoms
ANS – autonomic nervous system
BEAQ – Brief experiential avoidance questionnaire
CNS – central nervous system
ERQ – Emotion regulation questionnaire
ENS – enteric nervous system
FGD – functional gastrointestinal disorder
OGD – organic gastrointestinal disorder
PHQ – Physical health questionnaire
STAI – State-trait anxiety inventory

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