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Source / Izvornik: **Journal of Evidence-Based Psychotherapies, 2024, 24, 1 - 22**

Journal article, Published version
Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

https://doi.org/10.24193/jebp.2024.2.9

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:186:629495

Journal of Evidence-Based Psychotherapies,
Vol. 24, No. 2, September 2024, 1-22.

10.24193/jebp.2024.2.9

TEMPORAL DYNAMICS OF STRESS, AFFECT, AND ABDOMINAL PAIN IN IBS: INSIGHTS FROM A CLINICAL SAMPLE

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Abstract

Irritable bowel syndrome (IBS) has a complex aetiology involving biological and psychological alterations. Among others, stress seems to be a relevant factor for IBS symptom onset and exacerbation. Affective changes can be related to symptom severity and stressful experiences and may be valuable for therapeutic purposes. The aim of this study was to examine temporal dynamics of affect, stress, and symptom severity (specifically abdominal pain) in a sample of IBS patients.

Thirty-two outpatients kept a diary with a set of short questionnaires (Affect scale, Symptom severity scale, and Daily stress measure) once a day, in the evening, for 14 days.

Abdominal pain was modeled as a function of between-person, concurrent and lagged within-person effect of stress and affect controlling for autoregressive pain effects. Positive and negative affect exhibited concurrent effects on abdominal pain while stress did not. Daily variation in positive affect was associated with a decrease in pain while the opposite was true for negative affect. Positive and negative affect models explained over 40% of the variation in daily abdominal pain. Even though the models had a good fit, the amount of variance explained by positive and negative affect alone was relatively small (~7%) with high interindividual heterogeneity.

It seems that day-to-day stress variations do not have a direct impact on abdominal pain, while affective dynamics appear closely related to pain variations.

Keywords: Irritable bowel syndrome, Affect, Symptom severity, Daily stress.

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Irritable bowel syndrome (IBS) is one of the most common functional gastrointestinal disorders, characterized by changes in stool frequency and/or appearance accompanied by pain and discomfort (Lacy et al., 2016). Most IBS patients are women (M:F=1:2) and the prevalence rates in developed countries vary from 4.6% to 9.0% (depending on the criteria used) (Palsson et al., 2020). Although IBS has been in the focus of research for several decades, some aspects of the disorder remain unknown.

The predominating theoretical framework used to describe IBS and its aetiology is the biopsychosocial model of health and disease (Van Oudenhove et al., 2016). In line with the model, IBS is the result of life-long interactions of genetically determined traits (eg. personality traits, hypothalamic-pituitary-adrenal (HPA) axis reactivity) and environmental factors (exposure to pathogens, early adverse events) (Hauser et al., 2014). This interaction results in short-term and/or long-term changes in brain-gut communication, which are enabled via several mechanisms (central top-down connections, HPA axis, autonomic system, immune system) (Kennedy et al., 2012). Genes and early experiences shape specific brain-gut phenotypes which express different responses to external influences in adulthood (Mayer et al., 2023). Research shows that this brain-gut-microbiota axis has bidirectional connections, meaning that a change in any component of the axis can lead to global dysregulation and symptoms such as those in IBS (Martin et al., 2018).

Although much remains to be elucidated regarding the aetiology of IBS, findings have provided relatively consistent data regarding some of its aspects. For example, most models attempting to describe the aetiology of IBS and maintenance of its symptoms include some aspects of stress (Mayer et al., 2023, Qin et al., 2014; Van Oudenhove et al., 2016). Some focus on stressful life events, others include stress related personality traits (neuroticism) or states (anxiety). Early life stress is also viewed as a significant factor for the development of the brain-gut axis, and thereby IBS. And finally, the impact of everyday stressors on symptom exacerbation is considered, along with coping strategies, cognitions and behaviours IBS patients use to deal with these stressors (Hauser et al., 2014; Kennedy et al., 2012; Martin et al., 2018; Mayer et al., 2023).

Research indicates that stress most probably does have an impact on symptoms via various mechanisms within the brain-gut (-microbiota) axis (Martin et al., 2018). Different aspects and measures of stress have been related to IBS patients' functioning. Even though there seem to be no differences between IBS patients and inflammatory bowel disease (IBD) patients, or healthy controls on reports of major life events (Blanchard et al., 2008; Kovács et al., 2007; Levy et al., 1997), it seems that IBS patients report a greater number of negative stressful events (Halpert et al., 2005; Parker et al., 2019; Van Oudenhove et al., 2016) and a lower number of positive events (Drossman et al., 1988). IBS patients also show a higher reactivity to stress (Mayer et al., 2001), report higher levels of perceived stress

(Weaver et al., 2018) and experience elevated levels of daily stress compared to healthy controls (Blanchard et al., 2008; Hertig et al., 2007).

There are multiple mechanisms of stress action, possibly involving HPA axis dysregulation - reflected in altered cortisol levels (Chang et al., 2009; Kennedy et al., 2014), autonomic dysfunction (Mazurak et al., 2012; Van Oudenhove et al., 2016), maladaptive coping strategies, and altered cognitions and behaviours (Lackner et al., 2022).

Research shows that even prenatal stress in mothers has an impact on the development of the brain-gut-microbiota axis in infants. Infants of mothers reporting higher stress and anxiety had reduced diversity of microbiota species as well as lower quantity of beneficial microbiota species. Animal models have shown that prenatal stress in the mother can lead to visceral hypersensitivity in the offspring (Zhou et al., 2023). Emotional abuse, physical punishment and general trauma in childhood are associated with a greater risk for developing IBS later in life, as well as a variety of other medical conditions (Rahal et al., 2020), including anxiety and depression. This is one of several overlapping characteristics of IBS patients and people suffering from affective disorders.

IBS patients have elevated levels of anxiety and depression compared to healthy persons (Lee et al., 2017) and compared to patients with similar diseases with clear organic pathology (Henningsen et al., 2003). They also tend to have comorbid psychiatric diagnoses, such as generalized anxiety disorder or major depressive disorder (Gros et al., 2009; Henningsen et al., 2003), however their anxiety and depression levels are lower than those found in psychiatric populations (Creed et al., 2006; Hood et al., 2008). A recent meta-analysis showed that IBS patients have three-fold increased chances of having anxiety or depression, compared to healthy controls (Zamani et al., 2019).

The possible impact of anxiety and depression on IBS is diverse. For example, anxiety and depression could mediate the relationship between stress and GI symptoms, which was proposed by Hertig et al. (2007) when they demonstrated that this relationship becomes non-significant after controlling for levels of anxiety and depression. Furthermore, anxiety could lead to changes in cognitive interpretations of GI sensations, which could cause an attentional shift towards bowel sensations. Focusing attention on the abdomen in combination with worry and anxiety could exacerbate symptoms, reinforcing anxiety and thus closing the vicious circle (Deary et al., 2007). Compared to those without, IBS patients with anxiety and depression have altered ANS function, higher somatic symptoms, visceral hypersensitivity and higher visceral (GI-specific) anxiety (Midenfjord et al., 2019).

IBS patients usually report daily stressful events as triggers of symptom exacerbation, however the symptoms themselves can also act as stressors (Qin et al., 2014). Most research on daily stress and symptoms provides evidence for such a reciprocal relationship. There seems to be some support for concurrent, and to a

lesser degree, delayed effects of stress on symptom severity and vice versa (Pletikosić et al., 2016). Results obtained by Levy et al. (1997) show a positive relationship between same-day stress and symptoms, but also an increase in these correlations when multiple-day data are averaged. Several other studies (Blanchard et al., 2008; Chan et al., 2019; Pletikosić et al., 2016) also reported delayed effects of daily stress on symptoms (and vice versa), but some were unable to replicate those results and found only concurrent effects (Vork et al., 2020). The inconsistencies in obtained results could be attributed to variations in methodology, with some researchers using weekly data (Blanchard et al., 2008), others using end-of-day diaries (Dancey et al., 1998; Levy et al., 1997) and more recent studies (Chan et al., 2019; Vork et al., 2020) employing experience sampling methodology (ESM). In some studies, different patterns of the stress-symptom relationship are reported for subsets of patients (Levy et al., 1997; Pletikosić et al., 2016). Most of them reported only concurrent effects, while others (Hertig et al., 2007; Suls et al., 1994) found no significant relationship between daily stress and symptoms.

Most studies on stress and mood in IBS use retrospective patient reports, which limits the interpretation of their relationship with symptoms and quality of life. Temporal dynamics of mood have been the focus of research only recently. Research shows that low psychological well-being is related to unstable, more variable, and inert emotions (Houben et al., 2015). Findings suggest that compared to healthy controls, anxious individuals experience greater variability and instability of anxious mood following negative events (Lamers et al., 2018). Compared to patients in remission and healthy controls, patients currently experiencing anxiety or depression have the highest affect instability in positive and negative affect (Schoevers et al., 2021). Considering that anxiety is a characteristic of IBS patients, it is reasonable to wonder whether these altered dynamical patterns are also present in IBS patients.

Disentangling the stress-mood-symptom relationship could be relevant for psychological interventions. However, to our knowledge, there is a single study exploring this relationship in IBS patients (Chan et al., 2019), which has shown that an increase in daily stress predicts a subsequent decrease in symptoms, while symptom severity predicts an increase in negative affect and daily stress. The counterintuitive relationship between stress and symptom severity was also found in a subset of patients in one of our previous studies (Pletikosić et al., 2016), however Vork et al. (2020) only reported significant concurrent associations between stress and symptoms. This study aims to expand and reexamine the findings by Chan et al. (2019) in several ways. First, we included patients with all predominating subtypes, not only IBS-D. Second, in order to avoid missing data which is typical for momentary assessment and leads to uneven intervals between consecutive measurement points, we chose a larger time interval between measurements, ensuring that participants have enough time and the proper surroundings to complete

the diary scales. Finally, we used validated questionnaires for measuring positive and negative mood in order to increase the validity of the measurement. Accordingly, the goal of this preliminary report was to examine the effects of mood and stress on abdominal pain in a small sample of IBS patients.

Method

Participants

In this study, we recruited outpatients from two medical centres: the Clinical Hospital Center in Rijeka (Department of Gastroenterology) and Clinical Hospital Center "Sveti Duh" in Zagreb (Referral centre for functional gastrointestinal diseases). A total of 40 patients diagnosed with IBS (Rome III) participated in the study, however due to incomplete diary data (n=4), psychiatric comorbidities (n=2), and no variability in one of the measured variables (n=2) analyses were performed on data obtained from 32 participants (81.5% female). Their age range was 21 to 80 (M=50,76; SD=14,51), most of them were married (55,3%), currently employed (55,3%) and had a high school (50,00%) or University education (36,8%).

Measures

Affect scale

Affect was measured using an abbreviated version of the Mood scale (Kardum et al., 1992) which has 15 items and measures two factors (positive and negative affect). Positive affect (PA) contains the following adjectives: benevolent, lively, active, happy, tolerant, cheerful, satisfied. The negative affect factor comprises the following: melancholy, fearful, rejected, isolated, scared, irritable, sad, angry. The participants' task was to mark the degree in which they feel a certain way (e.g. isolated) from zero (not at all) to four (I feel that way completely). By calculating the average response for items of each subscale (PA and NA), two final scores are obtained.

Symptom severity scale

The Symptom severity scale was constructed based on the Gastrointestinal Symptom Diary (Blanchard, 2001). The scale has eight symptoms (diarrhoea, constipation, abdominal pain, abdominal tenderness, nausea, belching, bloating and flatulence), and the participants' task is to rate the severity of each symptom from zero (absent) to four (debilitating). In this paper, only data for abdominal pain was used.

Daily stress

Daily stress was measured using a single-item measure, modified from Larsson et al. (2015) (sleep disturbances were left out of the description and the time frame was modified to suit the needs of the study): "Stress means a situation when a person feels tense, restless, nervous, or anxious. Have you experienced such a situation today? Mark how stressful the situation was (0 – I haven't experienced such a situation today; 4 – extremely stressful).

Procedure

The study was conducted from February to April of 2018, in the Clinical Hospital Center in Rijeka and the Clinical Hospital Center "Sveti Duh" in Zagreb. Participants took part in a larger study and completed a series of questionnaires and computerized tasks during two sessions. Between those sessions, participants kept diaries once a day, in the evening, for a total of 14 days. Measurements were taken once a day as a means of capturing day-to-day variations, but also minimizing the burden of continuous two-week measurements on participants. This paper focuses solely on the prospective diary data. Participants were provided with booklets containing the Symptom severity scale, Affect scale and Daily stress. Prior to the beginning of the two-week monitoring period, participants were individually given detailed instructions. Participants were explicitly instructed not to retrospectively input data if they missed a measurement point. They were also provided with a phone number and an email address where they could reach out at any time with questions or other inquiries.

Analytic approach

The main goal was to estimate the relationship of daily stress and affect with abdominal pain perception, as well as their temporal dependency. Because of the nested structure of the data (measurement points nested within individuals/ participants), analyses were made within a hierarchical linear modeling approach using the 'lme4' package (Bates et al., 2015) for the R statistical environment (R Core Team, 2020). With this approach we can estimate the variance that can be attributed to participant diversity, and at the same time we can estimate the effects of specific ratings (stress and affect) at each measurement point.

Due to a low subject number, separate models were fitted for daily stress, positive and negative affect respectively. To separate between-person and within-person effects of daily stress and affect, daily PA, NA and stress ratings were decomposed into individual level mean (i.e. between-person effects) and by-subjects deviation from the specific individual level mean (i.e. within-person effects) (Little et al., 2006). Temporal dependency of daily stress, affect and abdominal pain perception, was tested using lagged terms. To control for possible pain perseveration,

an autoregressive abdominal pain term was included in all models. The fitted models were compared to the unconditional model containing only random (by-subject) intercepts via likelihood ratio test while the estimates' confidence intervals were calculated using a bootstrap procedure with 5000 samples. To help compare model estimates with usual regression results, standardized parameters, conditional and marginal R^{2}` estimates (Nakagawa et al., 2017) were calculated.

Sample size estimation

The sample size was estimated by means of power analysis corrected for multilevel data (Cohen, 1992; Hox, 2010). For an approximate effect size of trait (0.50) (Blanchard et al., 2008; Pletikosić & Tkalčić, 2016) and state (0.30) (Dancey et al., 1998; Vork et al., 2020), a power of 0.80 and a two-tailed alpha of .05, the minimum *N* was 28.25 at level 2 (trait) and 84.07 at level 1 (state). After level 1 *N* was corrected for nestedness (14 ratings per participant and an *ICC* of 0.30), the resulting number of ratings (level 1 *N*) was 411.60. The sample used in the study consisted of *N*=32 (level 2) and *N*=448 (level 1).

Results

Correlations were estimated using hierarchical linear modeling. Reliabilities for all measures were estimated with variance components for the unconditional model extracted via hierarchical linear modeling as suggested by Revelle and Wilt (2017). Descriptives, correlations and estimated person-level reliabilities are presented in Table 1.

Table 1. Between- and Within-Person Descriptives for Daily Stress, Positive and Negative Affect and Abdominal Pain.

Variable	Between-person			*r*				Within-person	
	RkRN	Mean	*SD*	1	2	3	4	Mean	*SD*
1. PA	.91	2.43	0.45	-	-.51**	-.39*	-.20*	0.00	0.49
2. NA	.83	0.83	0.47	-.33*	-	.45**	.17*	0.00	0.47
3. Daily stress	.79	1.06	0.55	.16*	.55**	-	.04	0.00	0.87
4. AP severity	.91	1.16	0.79	.01	.24*	.18*	-	0.00	0.76

PA: positive affect; NA: negative affect; AP: abdominal pain; RkRN: Reliability over k Random Nested days, reliability was averaged over time; Correlations below the diagonal are between individuals, and correlations above the diagonal are within-individuals. * p<.05; ** p<.01

Pain severity was characterized by relatively low intensity and high variability between and within-individuals. Between-person averages of daily stress and negative affect were relatively low as well, while the within-person variability

of daily stress was quite pronounced (high *SD*). Despite the high within-person variability, daily stress and abdominal pain severity were not significantly related within-person. Positive affect showed a higher within-person than between-person correlation with other measures.

To predict abdominal pain severity, separate models were fitted and their global fit indicators, as well as comparisons with an unconditional null model, are presented in Table 2.

Table *2*. Fit Indices of The Tested Models (Stress; PA and NA) and Significance Testing Compared to the Null-Model

Models	*df*	*AIC*	*BIC*	log-likelihood	χ^2 (vs. null-model)	*df*(χ2`)	*p*
Null-model	3	1143.30	1155.61	-568.65			
Stress model	8	787.18	817.13	-385.59	366.12	5	<.001
PA model	8	873.79	904.70	-428.89	279.51	5	<.001
NA model	8	868.12	898.94	-426.06	285.18	5	<.001

The inclusion of abdominal pain autoregressive term and respective predictors (stress, PA, NA, respectively) significantly increased the model fit above mere pain inter-individual differences. The parameters of specific models are presented in Table3.

All models exhibited a fair fit (Conditional R^2 <0.40) even though the estimated effect of fixed parameters was relatively low (Marginal R^2 ~ 0.07). Autoregressive pain effects were significant with an estimated effect of 0.17 (a one-point increase in pain above the person mean has a carry-over effect of 0.17 to the next day). Although the stress model was significant as a whole, no significant stress-related estimates were found and most of the model fit is to be attributed to auto-regressive pain effects. It must be noted though, that the between-person stress estimates were close to significance suggesting that it might be possible that individuals with higher mean stress levels have higher pain levels as well. Positive affect showed a significant concurrent within-person effect with no significant lagged effects. An increase in daily PA is associated with a -0.31 decrease in abdominal pain severity. The between-person estimates were small (close to zero). At the same time, negative affect exhibited a significant positive concurrent within-person effect on abdominal pain severity (0.27) with no significant lagged effects. Similar to the stress model, the between-person estimates were marginally higher than other NA estimates (p~0.10) potentially suggesting a possible between-person effect on abdominal pain.

Table 3. Estimated Coefficients, Bootstrap 95% Confidence Intervals, and Variance Components of Stress, Positive and Negative Affect Models

		Estimate	*S.E.*	Bootstrap 95% C.I.	Std. Estimate	*t*	variance
Stress	Intercept	0.58	0.27	0.05 : 1.13		2.13	0.3677
	Autoregressive term	0.15	0.06	0.04 : 0.25	0.15	2.65	
	Between-person effects	0.39	0.22	-0.05 : 0.84	0.19	1.74	
	Within-person effects	0.04	0.05	-0.06 : 0.14	0.03	0.73	
	Lagged effects (-1)	-0.05	0.05	-0.16 : 0.05	-0.04	-1.09	
	Lagged effects (+1)	0.03	0.05	-0.06 : 0.13	0.03	0.66	
	Residual						0.5692
					Conditional R^2		0.44
					Marginal R^2		0.08
		Estimate	*S.E.*	Bootstrap 95% C.I.	Std. Estimate	*t*	variance
Positive affect	Intercept	0.93	0.66	-0.37 : 2.24		1.41	0.4120
	Autoregressive term	0.17	0.05	0.06 : 0.28	0.17	3.25	
	Between-person effects	0.03	0.27	-0.50 : 0.54	0.01	0.10	
	Within-person effects	-0.31	0.08	-0.46 : -0.14	-0.14	-3.80	
	Lagged effects (-1)	0.04	0.08	-0.12 : 0.20	0.02	0.52	
	Lagged effects (+1)	0.01	0.08	-0.15 : 0.17	0.01	0.09	
	Residual						0.5475
					Conditional R^2		0.46
					Marginal R^2		0.06
		Estimate	*S.E.*	Bootstrap 95% C.I.	Std. Estimate	*t*	variance
Negative affect	Intercept	0.75	0.24	0.27 : 1.22		3.08	0.3904
	Autoregressive term	0.16	0.05	0.06 : 0.27	0.16	3.05	
	Between-person effects	0.32	0.25	-0.17 : 0.80	0.14	1.26	
	Within-person effects	0.27	0.09	0.09 : 0.45	0.11	2.93	
	Lagged effects (-1)	-0.10	0.09	-0.28 : 0.09	-0.04	-1.04	
	Lagged effects (+1)	-0.01	0.09	-0.19 : 0.17	-0.01	-0.14	
	Residual						0.5564
					Conditional R^2		0.46
					Marginal R^2		0.07

Discussion

This study examined the concurrent and delayed effects of affect and stress on abdominal pain in IBS patients. The obtained results show that concurrent levels of positive and negative mood are related to pain intensity. Positive mood was negatively related to concurrent abdominal pain, while a positive association was found for negative mood. Those concurrent effects of positive and negative affect were relatively balanced in intensity. The mentioned results suggest that the impact of positive and negative affect on abdominal pain on a day-to-day basis is similarly important. No significant association was found between daily stress and abdominal pain, neither for concurrent nor for delayed effects. As already mentioned in the Results section, the between-person effects of stress on abdominal pain were higher than the other stress related model parameters and close to formally significant, suggesting a possible relation of average stress levels with interindividual differences in abdominal pain (people with higher stress levels tend to experience more abdominal pain).

To our knowledge, repeated assessment of positive and negative affect has previously been reported only in one prospective study in IBS patients (Chan et al., 2019), making this the second study exploring such temporal dynamics of affect. We obtained several noteworthy findings. First, we found significant negative correlations between concurrent positive and negative affect, which was also described by Chan et al. (2019). This has previously been reported for healthy subjects (Diener et al., 1984), especially in the context of momentary assessment. Even when measured retrospectively, positive and negative affect are increasingly more related as the respective time frames become shorter. This could imply that even though positive and negative affect can be unrelated on a general level, it is unlikely one can feel both positive and negative affect at the same moment, especially at a high intensity (Diener et al., 1984).

Our data also indicated that negative and positive affect were significantly associated with abdominal pain, similar to results provided by Chan et al. (2019). Higher negative and lower positive affect were related to higher abdominal pain. Unlike Chan et al. (2019) who reported that pain and other GI symptoms were related to affective states in subsequent time points, we found significant concurrent effects, while delayed effects were not significant. This is probably due to the fact that Chan et al. (2019) used momentary assessment and their time points were, at most, separated by several hours, while ours were measured at daily intervals. Taken together, these findings suggest that the association between mood and pain is temporally limited to several hours, which is reflected in significant within-day effects, but not in delayed cross-correlations of end-of day diary scores. Regardless

of the temporal relationship, this shows that abdominal pain has a significant impact on daily psychological functioning and wellbeing of IBS patients.

In the present study, significant concurrent associations of daily stress and mood were obtained. More precisely, as daily stress levels rose, IBS patients reported lower positive and higher negative mood. This was true for intraindividual as well as interindividual effects. Similar results were reported by the abovementioned study by Chan et al. (2019), however they only presented data for stress and negative mood. Findings obtained using end-of day diary data on healthy persons revealed the same associations for positive and negative affect with stress (Richardson, 2017). The correlation between stress and negative affect is well known and is especially pronounced in persons with high trait neuroticism, as their reactions to negative and stressful events tend to be more intense and aversive (Mroczek et al., 2004). It is well established that IBS patients represent one such group of people with high trait neuroticism (Hauser et al., 2014).

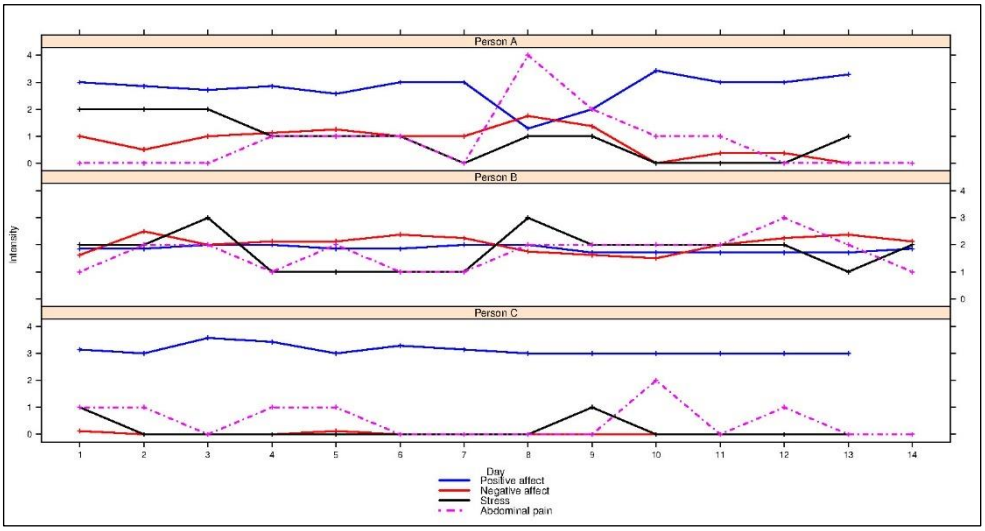

Figure 1. Positive and Negative Affect, Stress,
and Abdominal Pain Severity on 14 Days for Three IBS Patients.

Note: Patient A shows a relatively high variability and a visible association of affect, stress, and abdominal pain. Patient B shows a lower variability with lower and less clear associations of affect, stress, and abdominal pain. Patient C exhibits a low variability with an almost non-existent correlation of affect, stress, and abdominal pain.

The results of the present study do not support a significant relationship between daily stress and abdominal pain. We found no significant effects of stress on pain, neither concurrent nor delayed ones. This contrasts with findings by Chan

et al. (2019), who reported significant delayed effects, and Vork et al. (2020), who reported significant concurrent effects of stress on pain. In both of those studies, data were measured using momentary assessment, unlike our data which was reported retrospectively at the end of the day. It could be argued that stress and pain have an in-the-moment association, or a temporally limited association which is no longer significant when dealing with assessments for the experiences of an entire day. Mujagic et al. (2015) have shown that end-of-day diary abdominal pain scores are higher than scores obtained by momentary assessment, which could alternatively be the cause of these differing results. Perhaps the tendency of patients to overestimate pain intensity (which is a characteristic of persons with high neuroticism) leads to a distortion of the stress-symptom relationship, which is not the case for momentary assessment. Some previous studies which also used end-of-day diaries have reported significant associations of stress and pain in IBS patients. One study found correlations between symptoms and a combination of same-day and previous-day stress scores (Levy et al., 1997) and another found correlations between symptoms and a combination of stress scores from the preceding 4 days (Dancey et al., 1998). Both studies resorted to aggregated measures of stress, used small samples of IBS patients (n=26 and n=31) and reported significant associations in only 38% (Levy et al., 1997) and 43% (Dancey et al., 1998) of their participants. Similarly, Hertig et al. (2007) reported significant stress-symptom associations in around 30% of their sample (n=181), however these associations were substantially reduced after controlling for daily anxiety and depression. Their interpretation was that this relationship may be mediated by psychological distress, which we didn't measure directly in the present study, but it could be reflected in high negative and low positive affect. Thus, even though we did not find significant stress-symptom correlations, we did find significant stress-mood associations as well as mood-pain correlations, which supports the possible mediating effect of psychological distress in the stress-symptom relationship. Another marginally non-significant effect is worth mentioning, especially considering the limited size of our sample – the average bi-weekly stress level reflected in interindividual variations of stress was marginally related to abdominal pain (p=0.18). This average of daily assessments could be viewed as a measure of chronic stress, which would imply that IBS daily symptoms are most dominantly impacted by long-term or chronic exposure to daily stress.

In line with our findings, Suls et al. (1994) reported no significant effects of daily stress on symptoms after controlling for autocorrelation of symptoms, but they found significant stress-symptom correlations of weekly aggregates. Similarly, Blanchard et al. (2008) also analysed weekly data and concluded that most of the evidence supports a reciprocal relationship between stress and symptoms, rather than a causal one. They offered a very plausible explanation as to why patients so often report stress as a precursor to symptom exacerbation: one cannot separate the concurrent stress-symptoms effects, from the delayed stress-stress and symptoms-

symptoms effects, and by integrating them into one experience, it seems as if stress precedes and exacerbates symptoms. Whether or not stress and symptoms have a causal relationship, remains to be elucidated. Perhaps the answer will not be straightforward – we might find that such a relationship exists not for all, but for some of the patients, or not consistently, but some of the time. Such heterogeneity in the magnitude of associations between stress and abdominal pain between participants was present in our data. It was also reported by previous studies (Vork et al., 2020), and evident from stress-symptom correlations having been reported only for subsets of IBS samples (Dancey et al., 1998; Hertig et al., 2007; Levy et al., 1997). In the present study this heterogeneity was illustrated in Figure 1 which presents data from 3 IBS patients with different affect and stress-pain associations over the 14-day period. The observed heterogeneity could be the result of several different factors, for example differences in how people experience stress (physiologically and psychologically) and how they cope with the stress they have experienced. First, patients who are physiologically less responsive to stressful stimuli may not experience a significant effect of those stimuli on their abdominal symptoms. Reported variations in findings on autonomic and HPA axis functioning in IBS patients offer evidence of such interindividual differences (Böhmelt et al., 2005; Kennedy et al., 2014; Mazurak et al., 2012). Secondly, considering that we did not measure physiological stress, but rather perceived stress, we must acknowledge that there are differences in what people report as stressful (Mroczek et al., 2004). Third, interindividual differences in how people deal with the experience of stress are best described using coping strategies. Findings reported by Lackner et al. (2010) indicate that IBS patients who employ more effective coping strategies could in effect be buffering the effects of stress on their symptoms, or specifically, their abdominal pain. And finally, there are different types of stressors which can have different effects on symptom generation and perpetuation (Mayer et al., 2001), which we did not control for in the present study.

The main limitations of this study are its correlational nature, which does not allow for making causal inferences on the nature of the stress-symptom relationship and the relatively small sample size. Also, end-of day retrospective diary assessment might not be the most appropriate method for capturing stress-symptom associations. Considering all of the above, the conclusions of this study are limited. However, prospective studies of this type are rare due to the level of engagement which is required from the patients and the time it takes for data collection, thus the contribution from this clinical sample might be valuable for directing future research.

Clinical implications of this study are in line with previous research, despite the small sample size. Although the results indicate that there are no correlations between day-to-day stress and abdominal pain in IBS patients, and only point to a marginal effect of average stress on average pain scores, this does not mean that stress is irrelevant for IBS. On the contrary, research indicates that the impact of

stress on IBS outcomes (quality of life, burden of illness, symptom severity) is more indirect than direct - through cognitive and behavioural processes which maintain symptoms. For example, it seems that maladaptive coping strategies (rigid coping style accompanied by problem focused strategies) related to cognitive alterations (impaired cognitive flexibility and problem solving) and negative mood (worry, anxiety, catastrophizing) are especially important for IBS. Cognitive-behavioural therapies (CBT) which focus on these mechanisms seem to be most effective and have a long-lasting impact on the improvement of IBS symptoms (Lackner et al., 2022). Meta-analyses show that psychotherapy in general is effective for reducing various psychosocial symptoms in IBS patients, including anxiety, depression, and catastrophizing, but most importantly, psychotherapy leads to a reduction in GI symptoms (Black et al., 2020; Hetterich & Stengel, 2020). CBT interventions (specifically minimum contact CBT, standard CBT and group CBT) have the most consistent effects, and have been shown to be more effective than active control programs (such as psychoeducation) which also have some positive effects on treatment outcomes (Black et al., 2020). In addition to symptom reduction, CBT results in significant improvements in psychosocial functioning of IBS patients, including quality of life, visceral anxiety and negative cognitions (Craske et al., 2011; Ljótsson et al., 2011).

Specific therapeutic techniques which simultaneously lead to improvements in psychosocial outcomes (stress, quality of life) and symptom-related outcomes (pain, bowel dysfunction, symptom severity), some of which are utilized in CBT, include: support or empathy, symptom self-monitoring, self-monitoring of cognitions, finding associations between symptoms and cognitions, providing feedback, problem solving, encouraging rehearsal. It also seems that explaining the working mechanisms of an intervention improves its effectiveness (Henrich et al., 2015, Hetterich & Stengel, 2020). For detailed information on CBT for IBS, see Lackner (2020).

From the CBT perspective, it is the interpretation of events, not the events themselves, which increases the intensity of negative emotions and feelings, negative thoughts, and physical symptoms such as pain. Teaching patients how to employ effective cognitive strategies in order to challenge their beliefs and attitudes about their own health leads to a change in the way patients interpret information. This is important especially for patients experiencing heightened stress, who see themselves as vulnerable and unable to cope with stressful events, which consequently leads to excessive worry about future events (for example, having bowel-related accidents in public). Worrying about events which are unlikely to happen is negatively reinforced by the events not occurring – which further increases worrying in the future. This vicious cycle of stress, negative emotions, symptoms and behaviour can be broken by challenging beliefs about future events, specifically by training patients to monitor and evaluate their own thoughts and feelings (Lackner, 2020). Our results

point to a marginally significant between-subject effect of stress on pain, in other words we found that patients with higher average stress levels seem to experience more pain. Based on the CBT approach, these patients may be interpreting their pain more intensely because of limited psychological resources and stress-related changes in mood (lower positive and higher negative mood). Applying CBT techniques based on the obtained results would indicate, for example, combining symptom self-monitoring (in order to detect what precedes symptoms and if any patterns exist) with relaxation training (with the aim of reducing physiological arousal) and flexible problem solving (teaching patients adaptive coping strategies – problem oriented in the case of controllable problems and emotion-oriented for uncontrollable problems) in order to reduce patients' stress levels, and consequently the level of reported pain. On a day-to day level, the obtained results underline the significance of low positive mood and high negative mood, which are both related to increased daily stress and increased daily pain levels. It could be proposed that employing emotion (and cognition) self-monitoring, combined with symptom self-monitoring, and making connections between the two, could be effective in pain reduction, and possibly daily stress alleviation in IBS patients (Henrich et al., 2015).

Authors' Notes

Funding: This study was financially supported by University of Rijeka (Grant Number 13.04.1.3.1).

Competing interests: The authors declare that there are no potential conflicts of interest associated with this publication, and that any financial support has been noted in the Acknowledgment section.

Ethics approval: This study was performed in line with APA ethical standards and the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committees of Clinical Hospital Centre Rijeka (February 6th, 2018.; Class 003-05/18-1/11, Reg. No. 2170-29-02/15-18-2) and Clinical Hospital Sv. Duh Zagreb (January 25th, 2018.; Reg. No. 01-384).

Consent: Informed consent was obtained from all participants included in the study.

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