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Prevalence and Risk Factors for Irritable Bowel Syndrome in Recovered and Non-recovered Borderline Patients over Ten Years of Prospective Follow-up

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Abstract

This study examined rates of irritable bowel syndrome (IBS) over 10 years of prospective follow-up among recovered and non-recovered patients with borderline personality disorder (BPD). Subsequently, risk factors for IBS were examined in female BPD patients. As part of the McLean Study of Adult Development, 264 BPD patients were assessed at baseline and their medical conditions and time-varying predictors of IBS were assessed over five waves of follow-up (from six-year follow-up to 16-year follow-up). Semistructured interviews were used to assess both our IBS outcome variable and our baseline and time-varying predictor variables. Rates of IBS were not significantly different between recovered and non-recovered borderline patients when men and women were considered together and when men were considered alone. However, a significant difference in IBS rates was found between recovered and non-recovered female BPD patients, with the latter reporting significantly higher rates. The rates of IBS in women with BPD were found to be significantly predicted by a family history of IBS and a childhood history of verbal, emotional, and/or physical abuse. Taken together, the results of this study suggest that both biological/social learning factors and childhood adversity may be risk factors for IBS in women with BPD.

Keywords

irritable bowel syndrome; borderline personality disorder; adversity; biology; social learning

Physiological complaints are common in BPD patients (Frankenburg & Zanarini, 2004; Sansone, Whitecar, Meier, & Murry, 2001; Sansone & Sansone, 2003; Tragesser, Bruns, & Disorbio, 2010; Sansone, Lam, & Wiederman, 2011). However, the occurrence of irritable bowel syndrome (IBS), a functional gastrointestinal disorder characterized by abdominal pain or discomfort and altered bowel habits (i.e., diarrhea, constipation) (Tanaka, Kanazawa, Fukudo, & Drossman, 2011) has not been examined. This is surprising as comorbidity of BPD symptoms with gastrointestinal disorders significantly worsens prognosis in terms of

quality of life and increases the likelihood of suicide attempts (El-Gabalawy, Katz, & Sareen, 2010).

Comorbidity between IBS and BPD is likely. First, BPD may predispose someone to develop IBS. As stress itself is an important contributor to exacerbation of IBS (Tanaka et al., 2011), the emotional instability and hypersensitivity related to BPD may make these patients more vulnerable to its exacerbations. In fact, physiological complaints can be viewed as a manifestation of the self-regulatory disturbances that are characteristic of BPD (Sansone, et al., 2001; Tragesser et al., 2010). The co-occurrence of IBS and BPD may be most apparent in non-remitted BPD patients as studies have shown a link between BPD symptom severity and somatic comorbidity (Sansone, Wiederman & Monteith, 2001; Frankenburg & Zanarini, 2004; Frankenburg & Zanarini, 2006a; Frankenburg & Zanarini, 2006b).

Second, co-occurrence can be due to shared risk factors. Life adversities are common in IBS patients' history, ranging from abuse and neglect (e.g., sexual, physical abuse) (Salmon, Skaife, & Rhodes, 2003; Ross, 2005; Paras et al., 2009; Wilson, 2010; van Tilburg et al., 2010) to more subtle forms of maltreatment (e.g., hostility) (Lackner, Gudleski, & Blanchard, 2004). Drossman (1998) proposed that co-association between an abuse history and medical conditions is related to a variety of adverse clinical consequences, including both IBS and BPD. Indeed, a history of life adversities is also common in BPD patients (Zanarini, Gunderson, Marino, Schwartz, & Frankenburg, 1989; Zanarini et al., 1997; Sansone, Hahn, Dittoe, & Wiederman, 2011).

Third, if BPD and IBS have a high co-occurrence, this might be explained, at least in part, by biological mechanisms that are involved in both disorders. Both IBS and BPD have been linked to serotonin and dysregulation of the HPA-axis (Tanaka et al., 2011; Levy et al., 2006; Ni et al., 2006; Maurex, Zaboli, Öhman, Asberg, & Leopardi, 2010; Zimmerman & Choi-Kain, 2009). Thus, there might be a shared biological contribution to both disorders.

The present study examined co-occurrence of BPD and IBS in recovered vs. non-recovered BPD patients. It was hypothesized that IBS would be more common among the latter group. Furthermore, adulthood and childhood adversities, and a family history of IBS were hypothesized to heighten the risk for developing IBS in these patients. Understanding this relationship is valuable as it may provide insight into the links between somatic and psychological complaints and lead to improvement of currently used treatments for both disorders.

Methods

The current study is part of a multifaceted longitudinal study of the course of borderline personality disorder--the McLean Study of Adult Development (MSAD). The methodology of this study, which was reviewed and approved by the McLean Hospital Institutional Review Board, has been described in detail elsewhere (Zanarini, Frankenburg, Hennen, & Silk, 2003). Briefly, subjects were initially inpatients at McLean Hospital in Belmont, Massachusetts. Each patient was screened to determine that he or she: 1) was between the ages of 18–35; 2) had a known or estimated IQ of 71 or higher; 3) had no history or current symptoms of an organic condition that could cause psychiatric symptoms, schizophrenia, schizoaffective disorder, or bipolar I disorder; and 4) was fluent in English.

After the study procedures were explained, written informed consent was obtained. Subsequently, each patient met with a masters-level interviewer blind to the patient's clinical diagnoses for a thorough diagnostic assessment. Three semi-structured diagnostic interviews were administered. These diagnostic interviews were: 1) the Structured Clinical

Interview for DSM-III-R Axis I Disorders (SCID-I) (Spitzer, Williams, Gibbon, & First, 1992), 2) the Revised Diagnostic Interview for Borderlines (DIB-R) (Zanarini, Gunderson, Frankenburg, Chauncey, 1989) and 3) the Diagnostic Interview for DSM-III-R Personality Disorders (DIPD-R) (Zanarini & Frankenburg, 2001). The inter-rater and test-retest reliability of all three of these measures have been found to be good-excellent (Zanarini & Frankenburg, 2001; Zanarini, Frankenburg, & Vujanovic, 2002). In addition, the Background Information Schedule (BIS) was used to obtain essential demographic, psychosocial, and treatment information about the patients. Both interrater reliability and validity of this instrument are satisfactory (Zanarini, Frankenburg, Khera, & Bleichmar, 2001).

Childhood history of pathological and protective experiences, and adult experiences of adversity were assessed by a second rater blind to all previously collected information. Childhood experiences were assessed using the Revised Childhood Experiences Questionnaire (CEQ-R) (Zanarini et al., 1997) and adult experiences were assessed using the Abuse History Interview (AHI) (Zanarini et al., 1999). The inter-rater reliability of these interviews has also been found to be good-excellent (Zanarini, Frankenburg, Reich, Hennen, & Silk, 2005). The Medical History and Services Utilization Interview (MHSUI), a semi-structured interview first introduced at the six-year wave of follow-up, was used to assess the presence of IBS. To be included, a medical diagnosis had to be given to the patient by a physician. The MHSUI has been validated by comparing patients' self-report with pre-existing medical records (Frankenburg & Zanarini, 2004). Kappa values obtained for any serious medical condition, and any serious medical condition in first-degree relatives, were 0.91 and 0.77 respectively. Kappa values for specific medical conditions ranged from 0.45 to 1.0, with a median of 1.0 (Frankenburg & Zanarini, 2004).

At each of five follow-up assessments, separated by 24 months, axis I and II psychopathology was reassessed via interview methods similar to the baseline procedures by staff members blind to baseline diagnoses. After informed consent was obtained, our diagnostic battery was readministered (with the SCID I focusing on the past two years and not as at baseline, lifetime axis I psychopathology). The follow-up inter-rater reliability (within one generation of follow-up raters) and follow-up longitudinal reliability (from one generation of raters to the next) of these three measures have also been found to be good-excellent (Zanarini & Frankenburg, 2001; Zanarini, Frankenburg, & Vujanovic, 2002).

Log linear regression models, fitted by generalized estimating equations, with diagnosis and time as main effects, were used in longitudinal analyses of IBS prevalence data. Tests of diagnosis by time interactions were also conducted. The analyses modeled the log prevalence of IBS, yielding an adjusted risk ratio (RR) and 95% confidence interval (95% CI) for diagnosis and time. Generalized estimating equations were also used to determine significant bivariate and multivariate risk factors for IBS. Alpha was set at the $p < 0.05$ level, two-tailed.

Results

Two hundred and sixty four patients met both DIB-R and DSM-III-R criteria for BPD at baseline (six-year follow-up). Of these 264 patients, 150 BPD patients achieved recovery, while 114 BPD patients did not. Recovery was defined as concurrent remission of BPD symptoms as well as having good social and vocational functioning during the previous two years (Zanarini, Frankenburg, Reich & Fitzmaurice, 2010; Zanarini, Frankenburg, Reich & Fitzmaurice, 2012). We defined remission as no longer meeting study criteria for borderline personality disorder for a period of two years or more (or at least one follow-up period). We defined good social and vocational functioning as having at least one emotionally sustaining

relationship with a close friend or life partner/spouse, and being able to work or go to school consistently, competently, and on a full-time basis.

Overall, 81% (N=213) of the subjects were female and 88% (N=231) were Caucasian. Subjects' average age was 33 years (SD=5.8), the mean socioeconomic status was 3.4 (SD=1.4) (where 1=highest and 5=lowest), and their mean GAF score was 54 (SD=13.2) (indicating moderate impairment in several areas, such as work or school, family relations, judgment, thinking, or mood). Significant differences between recovery groups were found for age ($t=4.96$, $df=262$, $p<0.001$), socioeconomic status ($t=11.10$, $df=262$, $p<0.001$), and GAF score ($t=-16.24$, $df=262$, $p<0.001$). More specifically, non-recovered borderline patients were significantly older (mean of 35 [SD=5.7] vs. 32 years [SD=5.5]), had a significantly lower socioeconomic status (mean social class 4 [SD=0.9] vs. 3 [SD=1.4]), and had a significantly lower GAF score (mean of 43 [SD=7.9] vs. 62 [SD=10.3]) than recovered borderline patients. In terms of continuing participation, 255 BPD patients were reinterviewed at 8 years, 249 at 10 years, 244 at 12 years, 238 at 14 years, and 231 at 16 years.

Table 1 shows the IBS rates over time between recovered and non-recovered BPD patients. When comparing recovered vs. non-recovered BPD patients, no significant difference was found between the two groups ($RR=0.71$, $P=0.088$). For both groups, the rates of IBS declined significantly over the 10 years of follow-up. A formal comparison between males and females for the effect of recovery on IBS was conducted via a test of interaction. This test was non-significant ($Z=-0.78$, $p=0.44$). This finding indicates that, when looking at the whole sample, the effect of recovery on IBS rates is not different between the 4 subgroups (i.e., recovered males, non-recovered males, recovered females, and non-recovered females). When men and women were analyzed separately, significant differences were found between recovered and non-recovered females ($RR=0.65$, $P=0.046$), but not between recovered and non-recovered males ($RR=0.96$, $P=0.940$).

The following analyses were therefore confined to female BPD patients. At 6-year follow-up, 18.2% of the 88 non-recovered BPD females had a diagnosis of IBS. Over the decade of prospective follow-up, this rate increased to 29.7%. Of the 125 recovered BPD females, 16% met diagnosis for IBS at 6-year follow-up, while this percentage remained relatively stable over time (15.8% at 16-year follow-up).

The percentage of female BPD patients reporting a history of childhood sexual abuse at baseline was 68.5%. BPD patients' average score on a composite variable aggregating childhood verbal, emotional, and/or physical abuse was 7.3 (SD=5.3, range=0–18) at baseline. The mean score for our aggregate childhood neglect score was 15.6 (SD=10.7, range=0–42).

Table 2 shows the prevalence rates of IBS in first-degree relatives and the mean (SD) of a composite variable measuring the severity of adult adversity (i.e., adult history of emotional, verbal, physical and/or sexual assault) over time for women with BPD. The composite variable for adult adversity was created by adding the number of types of abuse experiences, providing a range of 0 to 4. Both predictors were measured every two years over a decade of prospective follow-up. Over time, approximately a steady 10.0% of the patients reported a family history of IBS. The mean score for adult adversity was 1.0 (SD=1.1, range=0–4) at 6-year follow-up. This variable was relatively stable over time.

Analyses were conducted to determine whether abuse and neglect in childhood, adversities in adulthood, and a family history of IBS were risk factors for higher rates of IBS in women with BPD. Initially, all variables were tested separately in bivariate analyses. The results can be found in Table 3. As can be seen, all predictor variables except for the variable assessing

the severity of adult adversity were significantly associated with the prevalence of IBS. More specifically, the presence of childhood sexual abuse increased a borderline woman's likelihood to have been given a diagnosis of IBS by 73%. Each five-unit increase in the scale for non-sexual childhood abuse was associated with a 27% increase in the likelihood to have been given a diagnosis of IBS. For childhood neglect, every ten-unit increase on the scale was associated with an increased likelihood of 25%. Each one-unit increase on the scale for adult history of emotional, verbal, physical and/or sexual assault was associated with a 9% increase in the likelihood to have been given a diagnosis of IBS. Lastly, the presence of a family history of IBS was associated with a 79% increase in the likelihood to have been given a diagnosis of IBS.

In subsequent multivariate analyses that included all the aforementioned variables (see Table 4), childhood verbal, emotional, and/or physical abuse ($RR=1.22$, $P<0.05$), and a family history of IBS ($RR=1.74$, $P<0.05$) were significantly associated with reporting IBS. Specifically, each five-unit increase in our scale of non-sexual childhood abuse, increased a female borderline patient's chances of having an IBS diagnosis by 22%. Furthermore, those women with BPD who reported having a first-degree relative that had IBS were 74% more likely to report IBS in adulthood.

There is a small literature suggesting that there is a heightened prevalence of IBS in eating-disordered patients (Dejong, Perkins, Grover, & Schmidt, 2011; Perkins, Keville, Schmidt, & Chalder, 2005). Using time-varying variables, we assessed the following eating disorders as bivariate risk factors for IBS in women with BPD: anorexia nervosa, bulimia nervosa, eating disorder not otherwise specified (EDNOS), and five types of EDNOS. None were found to be significantly related to the presence of a diagnosis of IBS (results not shown).

Discussion

A number of findings have emerged from this study. First, prevalence rates of IBS did not significantly differ between recovered and non-recovered BPD patients when gender was ignored. In addition, the interaction between gender and recovery did not have a significant effect on IBS rates. Nevertheless, when looking within each gender separately, significant differences were found within the group of female BPD patients, with the non-recovered females being more likely to report IBS than the recovered females. At 16-year follow-up, approximately 30% of the non-recovered females reported IBS as opposed to 15% of the recovered females. For men, 22% of recovered patients and 19% of non-recovered patients reported IBS at 16-year follow-up. Thus, IBS found in males does not depend on being recovered, while for females IBS does seem to be related to recovery of BPD. This is a new finding that warrants further attention.

Overall, the finding that IBS is more common in non-recovered BPD female patients is consistent with previous studies that examined medical comorbidities in BPD (Sansone et al., 2001; Frankenburg & Zanarini, 2004; Frankenburg & Zanarini, 2006a; Frankenburg & Zanarini, 2006b). A failure to remit from BPD has been related to the presence of comorbid axis I disorders, including anxiety disorders (Zanarini, Frankenburg, Hennen, Reich, & Silk, 2004a). Furthermore, anxiety has been proposed as a core feature of BPD (Silverman, Frankenburg, Reich, Fitzmaurice, & Zanarini, in press). As IBS is known to be a common comorbid syndrome in anxiety disorders (i.e., panic disorder, social phobia) (Levy et al., 2006; Clarke, Quigley, Cryan, & Dinan, 2009; O'Malley, Quigley, Dinan, & Cryan, 2011), higher comorbidity in those who fail to recover from BPD is not surprising.

When looking at the proposed risk factors for IBS in females, we found only the severity of a childhood history of non-sexual abuse (i.e., verbal, emotional and/or physical abuse), and a

family history of IBS to be significant predictors in multivariate analyses. That childhood sexual abuse, neglect, and adulthood adversities were not significant in the multivariate analyses of predictors of an IBS diagnosis is not completely in line with previous IBS studies. In fact, most support has been found for a relationship between IBS and childhood sexual abuse (e.g., Paras et al., 2009; van Tilburg et al., 2010), while support for a relationship between neglect and forms of adulthood adversity and IBS, although more limited, has also been found in previous studies (Leserman et al., 1996; Reilly, Baker, Rhodes, & Salmon, 1999; Heitkemper, Cain, Burr, Jun, & Jarrett, 2011). Further research is needed to address the exact role of these factors in the development of IBS.

The finding that a family history of IBS is among the strongest risk factors may indicate that the proneness of this subgroup to develop IBS may be due to a genetic vulnerability. Interestingly, it has been proposed that the subgroup of BPD patients that fails to remit is characterized by a strong temperamental component (Zanarini et al., 2004b). Such a component might also be at play in the subgroup of BPD patients that fails to recover. If so, this may explain the co-occurrence of IBS in these patients, as BPD symptom severity and the occurrence of somatic complaints have been related in previous studies (e.g. Sansone et al., 2001). However, the heightened risk of developing IBS in women with BPD who have a family history of the disorder may be due, at least in part, to social learning in the home environment. Gastrointestinal symptoms in family members, including the future patient, may be the object of strong parental interest and concern as well as a vigorous search for a medical explanation, treatment, and diagnosis.

This study has several limitations. First, study participants were seriously ill inpatients at the start of the study, with many of them being in therapy and taking psychotropic medication during the years of follow-up (Hörz, Zanarini, Frankenburg, Reich, & Fitzmaurice, 2010). Clearly, medication may influence certain somatic complaints. Furthermore, it is difficult to know if the results would generalize to a less disturbed group of patients or people meeting criteria for BPD who are not in treatment. Second, the sample of males was small, making the interpretation of the findings pertaining to them difficult to interpret due to a lack of statistical power. Third, all the data was collected by means of patient report of their physician's diagnosis of IBS. Our prevalence rates of IBS might have been different if we had had access to their medical records or had directly assessed each patient for IBS according to the Rome criteria (see Drossman, Corazziari, & Delvaux, 2006).

Taken together, our results highlight an important connection between a failure to recover from BPD and the presence of IBS in women. Furthermore, this relationship is associated with the severity of a childhood history of verbal, emotional and/or physical abuse, and a family history of IBS. Both disorders are frequently seen by psychiatrists, internists, and family physicians. Understanding the connection between the two disorders may help identify common developmental pathways and treatment approaches that can alleviate some of the suffering caused by these disorders.

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Table 1

Prevalence of Irritable Bowel Syndrome among Recovered and Non-recovered Borderline Patients over 10 Years of Prospective Follow-up

	Non-recovered Patients						Recovered Patients						Risk Ratio Diagnosis Time	95% CI Diagnosis Time
	6 Yr FU (N=114)	8 Yr FU (N=109)	10 Yr FU (N=105)	12 Yr FU (N=101)	14 Yr FU (N=98)	16 Yr FU (N=95)	6 Yr FU (N=150)	8 Yr FU (N=146)	10 Yr FU (N=144)	12 Yr FU (N=143)	14 Yr FU (N=140)	16 Yr FU (N=136)		
IBS in whole sample ^a	14.9 (17)	20.2 (22)	18.1 (19)	25.7 (26)	25.5 (25)	27.4 (26)	16.0 (24)	9.6 (14)	13.9 (20)	14.7 (21)	15.7 (22)	16.9 (23)	0.71 1.48 --	0.48, 1.05 1.09, 1.99 --
IBS in males ^b	3.9 (1)	12.0 (3)	8.0 (2)	17.4 (4)	19.1 (4)	19.1 (4)	16.0 (4)	12.0 (3)	20.8 (5)	8.7 (2)	9.1 (2)	22.7 (5)	0.96 1.64 --	0.32, 2.88 0.68, 3.98 --
IBS in females ^c	18.2 (16)	22.6 (19)	21.3 (17)	28.2 (22)	27.3 (21)	29.7 (22)	16.0 (20)	9.1 (11)	12.5 (15)	15.8 (19)	17.0 (20)	15.8 (18)	0.65 1.44 --	0.42, 0.99 1.05, 1.99 --

^a P-value for diagnosis= 0.088, P-value for time= 0.011

^b P-value for diagnosis= 0.940, P-value for time= 0.271

^c P-value for diagnosis= 0.046, P-value for time= 0.024

Table 2

Time-Varying Predictors of IBS in Women with BPD

Variable	6 Yr FU (Baseline) (N=213)	8 Yr FU (N=205)	10 Yr FU (N=200)	12 Yr FU (N=198)	14 Yr FU (N=195)	16 Yr FU (N=188)
Family History of IBS	12.7% (N=27)	9.3% (N=19)	8.5% (N=17)	12.1% (N=24)	11.3% (N=22)	11.2% (N=21)
Mean [SD] of Adult adversity (Range=0–4)	1.0 (1.1)	1.0 (1.1)	0.8 (1.0)	0.8 (1.0)	0.5 (0.9)	0.4 (0.9)

Table 3
Bivariate Predictors of Irritable Bowel Syndrome in Female Borderline Patients over 10 Years of Prospective Follow-up

Variable	Relative Risk	SE	Z	P	95% Confidence Interval
Childhood Sexual Abuse *	1.73	0.47	2.01	<0.05	1.01, 2.96
Mean Childhood Verbal, Emotional, and/or Physical Abuse Score /5 *	1.27	0.12	2.43	<0.05	1.05, 1.54
Mean Childhood Neglect Score/10 *	1.25	0.12	2.26	<0.05	1.03, 1.51
Adult History of Emotional, Verbal, Physical and/or Sexual Assault (Range=0-4)	1.09	0.06	1.63	0.103	0.98, 1.21
Family History of IBS	1.79	0.31	3.41	0.001	1.28, 2.51

* Baseline predictors; others are time-varying

Table 4
Multivariate Predictors of Irritable Bowel Syndrome in Female Borderline Patients over 10 Years of Prospective Follow-up

Variable	Relative Risk	SE	Z	P	95% Confidence Interval
Mean Childhood Verbal, Emotional, and/or Physical Abuse Score /5*	1.22	0.12	2.00	<0.05	1.00, 1.49
Family History of IBS	1.74	0.30	3.25	0.001	1.25, 2.44

* Baseline predictor; other is time-varying