# Panic Disorder and Quality of Life: Variables Predictive of Functional Impairment

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**Objective:** The authors sought to characterize the functional impairment in patients with panic disorder, specifically the variance in impairment explained by demographic and clinical variables. Method: Sixty-two patients with panic disorder and 61 comparison subjects from three primary care clinic sites were assessed with an adapted form of the Structured Clinical Interview for DSM-III-R. Impairment was assessed according to three measures from the 36-item Short-Form Health Survey (general health perception, mental health, and physical functioning) as well as a principal component factor of the survey. Subjects were also compared with respect to personality variables, presence and severity of chronic medical illness, and demographic characteristics. Stepwise multiple regressions with and without pairwise interactions were used to construct models of disability in the patients with panic disorder. <u>Results:</u> The patients with panic disorder were more impaired than comparison subjects on each measure of the Short-Form Health Survey. The panic disorder diagnosis combined with major depression, increasing neuroticism and age, less education, and an interaction between panic disorder and age accounted for 48%–77% of the variance in impairment scores. Gender and ethnicity contributed modestly to the variance in impairment in physical functioning, whereas no contribution was demonstrated for chronic medical illness or city of residence. <u>Conclusions:</u> Factors in addition to panic phenomena contribute to the severe impairment seen in patients with panic disorder. Further research about factors that affect impairment may help improve clinical approaches to this illness.

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**P** anic attacks are highly prevalent in the United States (1), and 5%-8% of patients who present to primary care suffer from panic disorder; many more have infrequent panic attacks (2). People with panic attacks have a higher degree of functional disability than subjects without panic attacks (3). Panic disorder patients tend to be high users of health care services (3, 4), and they perceive their physical and emotional

health to be much worse than comparison subjects (3, 5). They are also at higher risk for substance abuse, suicide attempts, marital problems, and financial dependency (6, 7).

Leon and colleagues (8) analyzed the relationship between DSM-III-R symptoms in patients with panic disorder and functional impairment as measured by the Sheehan Disability Scales (9). The three clinical variables that were measured (frequency of attacks, percentage of time spent worrying about attacks, and degree of phobic anxiety) accounted for 37% of the variance in impairment, while the number of criterion symptoms during an attack and fear intensity did not add to impairment. Leon et al. concluded that DSM-III-R criteria account for less than half of the impairment experienced by patients with panic disorder and that other variables need to be studied (8).

It is not known what other variables account for the impairment in patients with panic disorder. Other psychiatric disorders frequently coexist with panic. Between 44% and 91% of patients with panic disorder have major depression (10), and people with major de-

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pression have significantly worse perceived health and social and vocational functioning than patients with hypertension or diabetes (11). Of patients with panic disorder, 25%–75% have a concurrent personality disorder (12), and these patients have significantly more phobic avoidance, are less likely to respond to pharmacologic treatment (13, 14), and are more likely to have recurrent panic attacks (15). However, the unique contribution that comorbid axis I and II disorders provide to the impairment seen in patients with panic disorder is not known.

Medical comorbidity is also common in patients with panic disorder, and the unique contribution of the comorbid disorders in generating disability is not clear. How panic disorder and demographic variables, such as age, gender, level of education, and ethnicity interact to affect level of impairment is also unstudied.

The current study was carried out as part of the DSM-IV Panic Disorder Field Trial (16). The goal of the field trial was to develop criteria for panic disorder that captured the greatest number of patients with panic attacks who were significantly disabled by their symptoms. The current study had two primary aims. The first was to characterize more completely the impairment seen in people with panic disorder. The second was to identify other variables (psychiatric and medical comorbidity, demographic characterisitcs) in addition to the presence of panic disorder that add to the severe impairment seen in patients with panic disorder but not in a comparison group of subjects without panic.

#### METHOD

#### Subjects and Measures

Patients underwent an initial screening at three primary care clinics: a university family medicine residency clinic in Albuquerque, N. Mex., and health maintenance organization clinics in Seattle and Albany, N.Y. The screening consisted of the following two questions:

1. In the last 6 months have you had a panic attack when you felt frightened, anxious, or extremely uncomfortable?

2. In the last 6 months have you had a sudden episode of rapid or irregular heartbeat?

Patients with a positive response to either of these questions were then queried about their attacks. The purpose of this initial screening was to find cases of two different subgroups of patients that could be compared: 1) patients who during the previous 6 months experienced one or more panic attacks that were characterized by at least four autonomic symptoms, and 2) primary care comparison subjects who had never experienced a panic attack.

All patients with at least one panic attack that consisted of four or more autonomic symptoms in the previous 6 months were offered a second-stage interview, as were patients who did not report having a panic attack within the previous 6 months. The second-stage interview was completed by 172 subjects. Twenty-four subjects had limited-symptom attacks or attacks in the past only and not in the previous 6 months; these subjects were excluded from the study. Of the remaining 148 subjects, 87 had experienced one or more panic attacks in the previous 6 months, and 61 were comparison subjects who, while they may have had other psychiatric disorders, had never experienced a panic attack. Subjects with a primary psychotic disorder or a current substance use disorder were excluded. The interviews occurred after the subjects had been given a complete description of the study and had provided written informed consent. All subjects were assessed with the following instruments at the second-stage interview:

1. The Structured Clinical Interview for DSM-III-R, to assess psychiatric diagnoses (17, 18).

2. The 36-item Short-Form Health Survey, which was validated in the Health Insurance Experiment and Medical Outcomes Study (19). The survey assesses patients' perceptions of their health-related quality of life and functioning across eight conceptual measures: physical functioning (the extent to which health limits physical activities), role functioning—physical (the extent to which physical health interferes with work or other daily activities), role functioning—emotional (the extent to which mental health interferes with daily activities), social functioning, bodily pain (the effect of pain on work), mental health, vitality, and general health perception. Subscales are scored from 0 to 100; higher scores indicate a more optimal health status.

3. The DSM-IV Panic Disorder Field Trial Core Assessment Schedule (16), a semistructured interview developed for the field trial that assesses 1) panic attack frequency and panic-related impairment for the previous 6 months; 2) DSM-IV and ICD-10 panic disorder and agoraphobia criteria; and 3) all treatment seeking for the previous 6 months.

4. The NEO Personality Inventory (20), a 60-item inventory of five factors: neuroticism, extroversion, conscientiousness, openness, and agreeableness. The dimension of neuroticism, used in the current study, measures high negative emotionality, worry and nervousness, insecurity, inadequacy, and hypochondriasis. People who score high in this dimension do not necessarily have a psychiatric disorder (20).

5. Chronic Disease Score (21), a measure of chronic medical illness derived from the patient's use of prescriptions over a 6-month period. This score is stable over a 1-year period and has a high correlation with physician ratings of severity of medical illness. It has also been found to predict hospitalization and mortality in the year after assessment when age, gender, and health care visits are controlled.

6. Other instruments administered at the second-stage interview, but not used for the current study, were the Sheehan Disability Scales (9) and the Disability Days Questionnaire (22).

Patients were characterized as having panic disorder if they met DSM-III-R or the proposed DSM-IV criteria. Sixty-two of the 87 patients with one or more panic attacks in the previous 6 months met these panic disorder criteria.

#### Statistical Analysis

This report includes data from the 62 subjects with panic disorder and 61 comparison subjects in the field trial. Nine independent variables were chosen to assess variance in impairment: age, gender, ethnicity (Caucasian non-Hispanic versus Caucasian Hispanic and other), years of education, current panic disorder, current major depression, significant medical illness (chronic disease score of 2 or higher), neuroticism, and the site from which the patient was recruited in the field trial (for this variable, data for Seattle and Albany were combined because there were only a few Albany subjects). These variables were chosen a priori on the basis of past work in the field and because of clinical relevance.

The 36-item Short-Form Health Survey was used as the impairment measure. There was a high correlation among all eight subscales, so we limited our analyses to the three measures that were most relevant and that had continuous data points (physical functioning, general health perception, and mental health). We also included a principal component factor (factor 1), which provided a good empirical summary of all 36 items by reducing them to fewer items with a high intercorrelation and was thus assumed to represent a general disability construct. Two subsequent factors not used here extracted the items that were uncorrelated.

After analyzing the demographic and general impairment data between groups, we performed a stepwise multiple regression analysis to determine how much of the variance in disability scores was accounted for by our nine variables. This main effects model included both study groups. Statistical significance was set at p<0.05.

The next procedure was a stepwise multiple regression analysis with interactions constructed in a pairwise manner, with a backward elimination procedure. This interactive model also included both TABLE 1. Impairment Scores of Patients With Panic Disorder and Comparison Subjects

	Score						
	Patient	Compa	Comparison				
	Panic D	Subj	Subjects				
	(N=	(N=	(N=61)				
Measure <sup>a</sup>	Mean	SD	Mean	SD			
General health	$51.8^{b} \\ 45.0^{c} \\ 71.0^{d}$	24.1	79.2	17.8			
Mental health		18.7	75.5	19.1			
Physical functioning		25.0	91.1	12.4			

<sup>a</sup>From the 36-item Short-Form Health Survey (19).

<sup>b</sup>Significantly greater impairment than comparison subjects (t=7.18, df=121, p<0.01).

<sup>c</sup>Significantly greater impairment than comparison subjects (t=8.96, df=121, p<0.01).

<sup>d</sup>Significantly greater impairment than comparison subjects (t=5.68, df=121, p<0.01).

study groups and was performed to determine if interactions between panic disorder and the other eight variables either added explanation of variance in disability scores or changed the variables that were found to be significantly associated with disability. Interactions were only considered significant at the p<0.01 level. We also calculated the effect size (beta) that our significant variables had in generating impairment.

The last procedure consisted of separate stepwise multiple regression analyses for the patients with panic disorder and the comparison subjects. This was done to investigate differences between the patients with panic disorder and comparison subjects for the main effects variables associated with impairment. With eight variables (panic disorder was not used) and group sizes of 62 and 61, respectively, these analyses may have low power for detecting true group differences.

# RESULTS

# Demographics and General Impairment

There were no significant differences between patients with panic disorder and comparison subjects in age (37.1 years [SD=11.2] versus 39.3 years [SD=12.9]) (t=0.99, df=121, p=0.33) or in the proportion with a high degree of chronic medical illness (19% [N=12] versus 11% [N=7]) ( $\chi^2$ =1.46, df=1, p=0.23). Patients with panic disorder were more likely to be female (82% [N=51] versus 62% [N=38]) ( $\chi^2$ =6.1, df=1, p<0.01), less educated (13.1 years [SD=3.0] versus 15.5 years [SD=3.7]) (t=4.00, df=121, p<0.01), and unemployed (24% [N=15] versus 7% [N=4]) ( $\chi^2$ =7.3, df=1, p<0.01); there was a trend for patients with panic disorder to be Caucasian Hispanic and other (35% [N=22] versus 20% [N=12]) ( $\chi^2$ =3.84, df=1, p=0.05).

Table 1 shows that patients with panic disorder had significantly more impairment than comparison subjects as measured by the general health, mental health, and physical functioning subscales of the 36-item Short-Form Health Survey. It is important to note that no impairment at all would be a score of 100 on each subscale, so our comparison subjects also endorsed some impairment. This was expected, since the comparison subjects were recruited from a primary care setting.

#### Impairment: Main Effects

Table 2 presents data from the main effects model, which used both study groups. Our nine main effect variables accounted for 54% of the variance in scores on the general health subscale. The five variables that were significant in accounting for this variance, and were thus associated with more impairment, were fewer years of education, a higher level of neuroticism, presence of major depression, increasing age, and presence of panic disorder. For the mental health subscale, our nine main effects variables accounted for 77% of the score variance. The two variables that were significant in accounting for this variance were a higher level of neuroticism and the presence of major depression. For the physical functioning subscale, the nine variables accounted for 48% of the variance in scores. The five variables that were significant in accounting for this variance were increasing age, fewer years of education, presence of major depression, being Caucasian non-Hispanic, and the presence of panic disorder. Finally, the nine variables accounted for 75% of the variance in impairment measured by the principal component factor (factor 1). The five variables that were significant in accounting for this variance were a higher degree of neuroticism, presence of major depression, presence of panic disorder, fewer years of education, and increasing age.

# Impairment: Interactions and Effect Sizes

Table 3 presents data from the interactive model, which also used both study groups. In this model, 57% of the variance in scores on the general health subscale was accounted for by our nine main variables and an interaction between panic disorder and age. This interaction indicates that subjects with panic disorder were more likely to endorse higher levels of impairment as age increased. The impairment in general health associated with panic disorder and age was partly represented in this interaction, which became the fourth of five variables that were significant in accounting for worse general health scores, along with fewer years of education, major depression, increasing age itself, and increasing neuroticism.

There were no significant pairwise interactions within the mental health subscale, so the main effects model was not altered by this procedure.

The panic-age interaction was again significant in predicting worse physical functioning, with the nine main variables and this interaction accounting for 53% of the variance in scores on the physical functioning subscale. This interaction also indicates that subjects with panic disorder were significantly more likely to endorse worse physical functioning as age increased. The panic-age interaction became the third of five variables that were significant in accounting for worse physical functioning scores, preceded by increasing age itself and fewer years of education, and followed by major depression and being Caucasian non-Hispanic. TABLE 2. Multiple Regression Analysis to Determine Amount of Variance in Impairment Scores Accounted for by Nine Main Effect Variables in 62 Patients With Panic Disorder and 61 Comparison Subjects

	Measure <sup>a</sup>								
	General Health $(R^2=0.54)$		Mental Health (R <sup>2</sup> =0.77)		Physical Functioning (R <sup>2</sup> =0.48)		Factor 1 <sup>b</sup> (R <sup>2</sup> =0.75)		
Main Effect Variable	F (df=1, 113)	р	F (df=1, 113)	р	F (df=1, 113)	р	F (df=1, 113)	р	
Panic disorder	5.13	< 0.05	0.86	0.36	3.93	< 0.05	17.26	< 0.01	
Major depression	8.38	< 0.01	13.51	< 0.01	7.02	< 0.01	21.36	< 0.01	
Neuroticism	10.19	< 0.01	87.25	< 0.01	2.45	0.12	23.41	< 0.01	
Chronic medical illness	0.37	0.54	0.82	0.37	1.59	0.20	0.95	0.33	
Gender (female)	0.58	0.45	0.35	0.56	1.33	0.25	0.33	0.57	
Ethnicity (Caucasian non-Hispanic)	0.03	0.86	0.37	0.55	3.99	< 0.05	0.15	0.70	
Age	7.75	< 0.01	0.55	0.46	17.83	< 0.01	8.76	< 0.01	
Years of education	11.34	< 0.01	1.25	0.27	13.56	< 0.01	12.73	< 0.01	
Residence (Albuquerque)	1.00	0.32	0.27	0.61	< 0.01	0.95	< 0.01	0.96	

<sup>a</sup>From the 36-item Short-Form Health Survey (19).

<sup>b</sup>Principal component factor derived by reducing the 36 survey items to a few items with a high intercorrelation to represent a general disability construct.

TABLE 3. Multiple Regression Analysis to Determine Amount of Variance in Impairment Scores Accounted for by Interaction of Panic Disorder With Other Main Effect Variables in 62 Patients With Panic Disorder and 61 Comparison Subjects

Variable	Measure <sup>a</sup>										
	General Health (R <sup>2</sup> =0.57)		Mental Health (R <sup>2</sup> =0.77)			Physical Functioning (R <sup>2</sup> =0.53)			Factor $1^{b}$ ( $\mathbb{R}^{2}$ -0.77)		
	F (df=1, 113)	р	Effect Size (beta)	F (df=1, 112)	р	Effect Size (beta)	F (df=1, 113)	р	Effect Size (beta)	F (df=1, 113)	<u>р</u>
Panic disorder	0.49	0.49		0.86	0.36		1.04	0.31		0.29	0.59
Major depression	10.77	< 0.01	$-15.2^{\circ}$	13.51	< 0.01	$-11.9^{\circ}$	9.35	< 0.01	$-13.0^{\circ}$	25.87	< 0.01
Neuroticism	8.64	< 0.01	$-0.6^{d}$	87.25	< 0.01	$-1.4^{d}$	1.57	0.21		21.49	< 0.01
Chronic medical illness	0.07	0.80		0.82	0.37		0.83	0.36		0.38	0.54
Gender (female)	1.51	0.22		0.35	0.56		2.77	0.10		1.12	0.29
Ethnicity (Caucasian non-											
Hispanic)	0.22	0.64		0.37	0.55		5.62	< 0.05	-8.3 <sup>c</sup>	0.48	0.49
Age	10.16	< 0.01	$-0.9^{e}$	0.55	0.46		22.18	< 0.01	$-1.0^{e}$	11.49	< 0.01
Years of education	13.36	< 0.01	$2.0^{\rm e}$	1.25	0.27		16.06	< 0.01	$2.0^{\rm e}$	15.05	< 0.01
Residence (Albuquerque)	1.35	0.25		0.27	0.61		0.01	0.94		0.04	0.85
Panic-age interaction	9.38	< 0.01	-0.8 <sup>e</sup>		n.s.		10.52	< 0.01	-0.8 <sup>e</sup>	10.07	< 0.01

<sup>a</sup>From the 36-item Short-Form Health Survey (19).

<sup>b</sup>Principal component factor derived by reducing the 36 survey items to a few items with a high intercorrelation to represent a general disability construct.

<sup>c</sup>Change in score if variable is present.

<sup>d</sup>Change in score for each point increase on the neuroticism subscale of the NEO Personality Inventory.

<sup>e</sup>Change in score for each additional year.

An optimal measure of overall impairment in our study was provided by the principal component factor. In the interactive model, 77% of the variance in factor 1 scores was accounted for by our nine main variables and an interaction between panic disorder and age. The five variables that were significant in accounting for this variance were the presence of major depression, a higher level of neuroticism, fewer years of education, increasing age itself, and the presence of panic disorder and increasing age, partly represented by the panic-age interaction.

Table 3 also shows the effect sizes of the variables that accounted for significant variance in impairment in the interactive model. As an example, the presence of major depression lowered the physical functioning score (signifying increasing impairment) by 13 points, being Caucasian non-Hispanic lowered the score by 8.3 points, each year of education raised the score by 2 points, and the variance accounted for by age that was represented in the panic-age interaction lowered the score by 0.8 points for each year of age. To clarify this interaction effect, a typical score on the physical functioning subscale for an 18-year-old patient with panic disorder was 88, which was similar to that of the comparison subjects. However, a typical score for a 38year-old patient with panic disorder was only 71, and a typical score for a 58-year-old patient with panic disorder fell further to 55. Figure 1 is a graphic example FIGURE 1. Interaction of Increasing Age and Level of Physical Functioning in 62 Patients With Panic Disorder and 61 Comparison Subjects



of this panic-age interaction regarding physical functioning. Comparison subjects in our study did not endorse worse functioning with increasing age within the age range studied.

# Panic Disorder Versus Comparison Subjects

When separate stepwise multiple regression analyses are performed for the patients with panic disorder and the comparison group, the panic diagnosis becomes a dependent variable. This allows for a description of how the groups differ in other factors associated with impairment. For the comparison subjects, a higher level of neuroticism (F=28.92, df=1, 52, p<0.01) and the presence of major depression (F=18.28, df=1, 52, p<0.01) were the variables associated with increasing impairment as measured by the factor 1 scale. For the patients with panic disorder, the variables associated with increasing impairment were fewer years of education (F= 17.96, df=1, 53, p<0.01), increasing age (F=17.23, df=1, 53, p<0.01), the presence of major depression (F=10.50, df=1, 53, p<0.01), and a higher level of neuroticism (F= 4.39, df=1, 53, p<0.05). In general, these data held true across the three subscales of the 36-item Short-Form Health Survey, except that for patients with panic disorder, being Caucasian non-Hispanic and male were also associated with significant impairment in physical functioning, but depression and neuroticism were not.

# DISCUSSION

This study is novel in determining that nine variables may account for as much as 77% of the variance in self-rated functional impairment in a group of patients with and without panic disorder. Patients with panic disorder had significantly more impairment than comparison subjects in the domains measured. These data corroborate other studies that have shown that people with panic disorder experience a high level of functional impairment. Our study differs from others in that it determines many of the specific sources of this impairment and their effect size.

This study addressed the complexity of impairment and quality of life in people with panic disorder. Variables associated with increasing impairment were dependent on specific disability constructs and accounted for between 48% and 77% of the variance in self-rated functional impairment. Our data indicated that impairment in patients with panic disorder was affected by the panic disorder diagnosis, psychiatric comorbidity (specifically, major depression), the personality dimension of neuroticism, age, education level, and the interaction between the panic disorder diagnosis and age. Gender and ethnicity were modestly associated with impairment only in physical functioning in patients with panic disorder. Chronic medical illness and city of residence were not risk factors for poor functioning in patients with panic disorder. Major depression and neuroticism significantly contributed to impairment in comparison subjects and in panic disorder subjects. Thus, variables that added to the greater impairment in panic disorder patients than in comparison subjects were the panic disorder diagnosis, age, education level, and modest input from gender and ethnicity.

The individual variables that significantly accounted for the variance in disability scores may have an effect size that is clinically significant (i.e., associated with significant life impairment). Ware et al. (23) reported that a 3-point decrease on the mental health subscale of the 36-item Short-Form Health Survey is an effect that occurs when one is fired or laid off from a job. Having major depression and a 3 of a possible 40-point increase on the neuroticism subscale of the NEO Personality Inventory had this effect in our study. If the same effect holds true for the general health subscale, then having major depression, a 5-point increase on the neuroticism subscale, 4 additional years of age, and 1.5 fewer years of education in patients with panic disorder would be similar to the loss of a job in terms of perceived life impairment.

Major depression and increasing neuroticism were found to be risk factors for a worse quality of life in our subjects. These data align with other studies that have shown that severe anxiety and depression are more predictive of social dysfunction than nonsevere anxiety and depression (24) and that panic patients with comorbid depression or personality disorder have worse treatment outcomes than patients with panic disorder alone (13, 25, 26). A lower education level was also found to be a risk factor for a worse quality of life in patients with panic disorder, but the reasons for this are not clear.

Clinicians are impressed by the variability between patients with similar levels of organic disease regarding

adaptation to the disease and levels of disability. There are also examples of nonpsychiatric illness in which disease severity has been shown to be only one of many factors that contribute to the degree of impairment that a patient experiences. Julius et al. (27) demonstrated this in a study of patients with end-stage renal disease. Harris et al. (28) compared patients with less severe chronic renal insufficiency to patients with other chronic medical illness and community subjects and reported that the renal patients had significant functional disability according to the Sickness Impact Profile (29). Extent of impairment was correlated with being white, female, poor, having less education and income, and having comorbid medical conditions but was not related to the level of renal function. Sullivan et al. (30) documented in a longitudinal study that functional status in patients with coronary artery disease was accounted for more by associated psychosocial variables than coronary artery disease severity itself. These authors have highlighted how concurrent problems detract from quality of life in patients more than does their identified clinical focus. Likewise, the current study highlights the complex nature of disability and quality of life in patients with panic disorder and underscores the need to assess the whole biopsychosocial milieu of the patient, regardless of the current focus of clinical attention.

Our patients were selected from primary care clinics, with the intent to case find for panic disorder, so the analyses may not be generalizable to other clinical or community populations. For example, the role of chronic disease in adding to the variance in impairment may be significant in other, sicker populations. However, the majority of people in the United States with panic disorder seek care in primary care clinics, and these people tend to be high users of care (4). Choosing a different comparison group may change our results, but we believe that the same primary care study group was the most appropriate. While ethnicity was not found to be a major risk factor for impairment, our study group was not very diverse. Almost all of the subjects lived in urban homes and were either Caucasian non-Hispanic or Caucasian Hispanic. A broader sample may yield different results. Statistical analyses with many variables introduces potential loss of power. With nine independent variables and a study group size of 123, our major analyses are adequate. Our withingroup analyses may have low power, but this would only cause an underestimation of the number of variables significantly associated with impairment. Introducing panic-specific variables to replicate the Leon et al. study (8) may have been useful but was not done because of this statistical limitation. Our analyses do highlight the importance of methodologic differences in making inferences about data. In this case, an interactive model more accurately reflects how panic disorder and age add to disability and that they are not completely independent predictors, as suggested by the main effects model. Our analyses do not allow for much inference about the qualitative association between our variables and impairment. For example, is the robust association between the panic-age interaction and impairment due to age alone or chronicity of an illness?

# CONCLUSIONS

The current study adds to the literature regarding the quality of life in panic disorder by determining many of the specific sources of functional disability. Impairment is complex and may be related to factors other than the illness that is the focus of a clinician's attention. This study raises questions that call for further research about the variables that we could and could not account for, the qualitative relationship between these variables and the impairment measures, and outcomes research when treatment is directed at all the variables that add to impairment. These studies may inform us more about the genesis of disability and how we might improve the quality of life in people with panic disorder.

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