Research / Araştırma

Relationship Between Empathic Responding and its Clinical Characteristics in Patients with Major Depressive Disorder

Okan Ekinci[1], Asli Ekinci[1]

[1]Usak State Hospital, Department of Psychiatry, Usak - Turkey

ABSTRACT

Relationship between empathic responding and its clinical characteristics in patients with major depressive disorder

Objective: To our knowledge, there is no study specifically examining the relation between empathic responding and clinical features in patients with major depressive disorder (MDD). Our aim was to examine cognitive and affective empathic responding in patients with MDD and to explore the possible relations between clinical features and empathy.

Method: The sociodemographic and clinical properties of 83 patients with major depression were recorded. The Beck Depression Inventory (BDI) was used to assess severity of depression, whereas the Beck Anxiety Inventory (BAI) was used to assess anxiety. Hopelessness level was measured by Beck Hopelessness Scale (BHS). Patients' empathic ability was evaluated by using the Interpersonel Reactivity Index (IRI), and results were compared with 85 healthy controls. We used Pearson correlation and general linear model analysis to evaluate the manner in which the variables contributed to the IRI scores.

Results: Perspective Taking (IRI-PT), Empathic Concern (IRI-EC), and Fantasy (IRI-FS) subscores were all substantially lower in subjects with depression than in healthy controls, while the Personal Distress (IRI-PD) subscore was higher than in healthy subjects. There were significant effects of gender on the scores of IRI-EC and IRI-FS. Lower IRI-FS and IRI-PD scores were found to be significantly related to high suicide risk in depression.

Conclusion: Based on our results, patients with major depressive disorder show significantly impaired empathy measures compared to the normal population. Our findings also suggest a close relationship between suicidality and empathy in patients with MDD.

Keywords: Empathy, gender, hopelessness, major depressive disorder, suicide

ÖZET

Majör depresif bozukluğu olan hastalarda empati yanıtı ve klinik özelliklerle ilişkisi

Amaç: Bildiğimiz kadarıyla majör depresif bozukluklu hastalarda empatik cevaplarla klinik özellikler arasındaki ilişkiyi araştıran herhangi bir çalışma yoktur. Amacımız majör depresif bozukluklu hastalarda duygusal ve bilişsel empati cevabını değerlendirmek ve empatinin klinik özelliklerle olan muhtemel ilişkisini araştırmaktır.

Yöntem: Majör depresif bozukluklu 83 hastanın sosyodemografik ve klinik özellikleri saptandı. Depresyon şiddetini ölçmek için Beck Depresyon Ölçeği, anksiyete şiddetini ölçmek için Beck Anksiyete Ölçeği kullanıldı. Umutsuzluk düzeyi Beck Umutsuzluk düzeyi ile ölçüldü. Hastaların empati yetenekleri Kişilerarası Tepkisellik İndeksi ile ölçüldü ve 85 sağlıklı kontrol ile karşılaştırıldı. Hangi değişkenin empati puanlarına ne yönde etki ettiğini değerlendirmek için korelasyon analizi ve genel lineer model kullanıldı.

Bulgular: Kişilerarası Tepkisellik İndeksi'nin Perspektif alma, Empatik düşünce ve Fantazi alt ölçek puanları depresif hastalarda kontrol grubuna göre anlamlı olarak daha düşükken, Kişisel sıkıntı alt ölçek puanları ise anlamlı olarak daha yüksekti. Cinsiyetin empatik düşünce ve fantazi alt ölçek puanları üzerinde anlamlı etkisi olduğu bulundu. Ayrıca depresyonlu hastalarda düşük fantazi ve kişisel sıkıntı skorlarının yüksek intihar riski ile ilişkili olduğu bulundu.

Sonuç: Bulgularımıza dayanarak depresif bozukluklu hastalarda normal popülasyona göre anlamlı olarak bozulmuş empati ölçümleri olduğu söylenebilir. Ayrıca bulgularımız depresif olgularda intihar ve empati arasında yakın bir ilişki olduğuna işaret etmektedir.

Anahtar kelimeler: Empati, cinsiyet, umutsuzluk, majör depresif bozukluk, özkıyım

Address reprint requests to / Yazışma adresi:
Okan Ekinci,
Usak State Hospital, Department of Psychiatry,
Fevzi Cakmak Mah., Denizli Cad. No: 4,
64200 Merkez/Usak, Turkey

Phone / Telefon: +90-276-224-0000

Fax / Faks: +90-276-224-0001

E-mail address / Elektronik posta adresi:
drokanekinci@yahoo.com

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INTRODUCTION

Empathy is a multidimensional construct referring broadly to the ability to infer and share the emotional states of others in reference to one's own (1). Theoretical models of empathy suggest that it is multidimensional and integrative in nature, consisting of both cognitive and affective components: a) the degree to which someone feels the emotions of another person (affective empathy), and b) the ability of deducing the other's mental state and intentions, often referred to as mentalizing (cognitive empathy) (2-4).

Major depressive disorder (MDD) is a common psychiatric disorder associated with significant impairment in daily functioning that often occurs in social cognitive areas. It is widely accepted that empathy is a complex construct and a key component of social cognition (5,6). In the context of major psychiatric disorders, empathy has been mostly studied in personality disorders, schizophrenia, and autism spectrum disorders. Although the relation between empathy and depression has been considered a significant feature, it has not been widely studied in major depressive patients (7-10). To date, studies examining empathy in MDD have been focused on the associations between the severity of psychopathology, social functionality, and empathy. The major limitation of these studies was that they did not consider possible associations between empathy, gender, and specific clinical features, although patients with MDD vary substantially in the presentation of their illness in relation to these variables (11-13). Thus, some clinical features, such as the presence of psychotic mood episodes and suicide attempts, may cause different disease courses in depressed subjects. In addition, the relationship between empathy and gender in patients with MDD is unclear, although the presence of this relationship in non-depressed people is most consistently supported by various studies (14,15).

To our knowledge, there is no study specifically examining the relation between clinical features and empathic responding in patients with MDD. In our study, we used the Interpersonal Reactivity Index (IRI) to assess empathic ability in order to find differences between (1) patients with MDD and healthy controls, and (2) depressive patients with different clinical properties. In addition, we aimed to determine the relationship between current suicidal risk and empathic responding in patients with depression. Our main hypothesis was that patients with MDD would have lower scores than healthy subjects on both affective and cognitive empathy subscales, and some clinical features would be differentially related to different empathy domains in subjects with depression. We also hypothesized that impaired empathic ability would be significantly related to high suicidal risk in depression.

METHOD

A total of 83 patients who met the DSM-IV criteria for MDD (16) were recruited at the outpatient service of our hospital. The study was approved by the Ethical Commitee. Before study-specific procedures were carried out, the study was thoroughly explained to the subjects, and written informed consent was obtained. Diagnostic interviews for the study group were conducted with the Turkish versions of the SCID-I and the SCID-II (17-20). Inclusion criteria consisted of being 18-55 years old and being diagnosed with MDD. Subjects who had other disorders that might influence cognitive function (significant neurological and physical illness, substance abuse or dependence in the last year, electroconvulsive therapy in the preceding year, intoxication or cerebral trauma history) and subjects who had comorbid axis I or II disorders were excluded. Our patient sample was also free from psychotic symptoms.

In addition, 85 control subjects matched for age, education and gender were tested. The control group comprised healthy volunteers with socio-cultural backgrounds similar to the patients'. Turkish versions of the Structured Clinical Interview for DSM non-patients (SCID-NP) and SCID-II were also administered to the control group (17,18), who did not have any current or lifetime axis I or II disorder. Controls conformed to the same exclusion criteria as the participants with MDD.

Clinical Assessment and Measures

The patient information form was specially designed by the authors for this particular study. Patients were examined in varying phases of illness to assess the relationship between symptom severity and empathic responding.

Beck Depression Inventory (BDI): The BDI was used to assess severity of depression. BDI is a 21-item self-report scale developed by Beck et al. (21) for evaluating the severity of depression. The Turkish version was reported to be valid and reliable by Hisli (22).

Beck Anxiety Inventory (BAI): The BAI was used to assess severity of anxiety. This is a self-report inventory with 21 items designed to evaluate the severity of physical and cognitive symptoms of individuals during the past week (23,24).

Interpersonal Reactivity Index (IRI): Empathy was measured by using the IRI, which is a 28-item self-report instrument that measures both cognitive and emotional aspects of empathy (2,25). Among self-reported psychological tests aimed at evaluating empathic functioning, IRI represents one of the most widely used and comprehensive instruments. Items are rated on a scale ranging from 0 (does not describe me well) to 4 (describes me very well). The cognitive subscales comprise the Perspective Taking (PT) and Fantasy Scales (FS). The PT subscale assesses the ability to take on the psychological point of view of others, allowing one to anticipate the behavior and reactions of other persons. This subscale is associated with emotional sensitivity. The FS subscale assesses the tendency to imagine oneself experiencing the feelings and behaviors of fictitious characters in books, movies, and plays, and may be related to imagination, general verbal intelligence, and the ability to engage others in social interaction. The Empathic Concern (EC) subscale measures the tendency to experience feelings of sympathy and concern for people in difficulty. Finally, the Personal Distress (PD) subscale assesses personal anxiety and discomfort experienced in emotional social settings (6,7). IRI is a valid and reliable instrument for Turkish healthy and psychiatric populations (25,26).

Beck Hopelessness Scale (BHS): Hopelessness level and the severity of current suicidal intent were measured using the BHS. This is a 20-item self-report scale assessing hopelessness/negative attitudes concerning coming events (27). The scale evaluates feelings about the future, loss of motivation, and expectations for the future. Subjects are requested to endorse a pessimistic sentence or deny an optimistic sentence. Beck et al. (28) conducted a follow-up study on 1958 outpatients and reported that those with higher BHS total scores were 11 times more likely to commit suicide than outpatients with lower BHS total scores. Thus, the BHS seems to be a useful predictor of eventual suicidal behavior. The present study used a cutoff score of ≥9 to identify patients at high risk for suicide as previously done in a study conducted by Pompili et al. (46). It is a valid and reliable instrument for Turkish healthy and psychiatric populations (28,29).

Statistical Analysis

We used the SPSS for Windows 16.0 version for all statistical analyses in this study. A confidence interval of 95% and a 2-tailed p value of less than 0.05 were considered statistically significant for all analyses. Variables were tested for homogeneity of variance by using the Levene test and for normality of distribution using the Kolmogorov-Smirnov test. For a comparison of sociodemographic characteristics of patients and controls, the χ^2 test was used. Bivariate correlations were computed to examine the relation between empathic responding, illness burden (e.g., depression severity, illness duration, age at onset of illness, number of depressive episodes). Alpha was set to 0.05 for all analyses. To determine the factors that are associated with empathy subscale scores, the data were analyzed using a multivariate analyses of variance (MANOVA), treating Group (MDD, HC) and gender as fixed variables and the score for each of the IRI subscales as a dependent variable.

Table 1: Demographic and clinical characteristics of subjects with major depressive disorder and healthy control subjects

	Major Depressive Disorder (n=83)		Healthy Controls (n=85)		
	Mean	SD	Mean	SD	p
Age	34.01	12.41	34.21	12.10	0.92
Length of education (years)	9.55	3.04	9.34	3.54	0.67
Age at illness onset	28.91	9.60	---	---	N/A
Duration of illness (years)	5.09	4.06	---	---	N/A
Number of hospitalizations	1.52	0.63	---	---	N/A
Number of depressive episodes	3.25	0.81	---	---	N/A
Beck Depression Inventory (BDI)	16.37	10.69	---	---	N/A
Beck Anxiety Inventory (BAI)	16.84	7.17	---	---	N/A
Beck Hopelessness Scale (BHS)	8.20	4.22	---	---	N/A
	n	%	n	%	p
Gender					
Female	60	72.3	49	57.6	0.05
Male	23	27.7	36	42.4	
Occupation					
Unemployed	10	12.0	9	10.5	0.42
Student	26	31.3	27	31.7	
Officer	14	16.8	13	15.3	
Retired	15	18.0	17	20.0	
Housewife	18	21.9	19	22.5	
Marital status					
Single	4	4.8	7	8.2	0.23
Married	72	86.7	65	76.5	
Widowed	7	8.4	13	15.3	
Smoking					
No	27	32.5	20	23.5	0.23
Yes	56	68.5	65	76.5	
Socioeconomic level					
Low	17	20.8	17	20.0	0.09
Medium	45	54.2	51	60.0	
High	21	25.0	17	20.0	
Family history of mental illness					
No	16	19.4	--	--	N/A
Yes	67	79.6			
Previous suicide attempt					
No	57	68.7	--	--	N/A
Yes	26	31.3			
Previous psychotic mood episode					
No	64	77.1	--	--	N/A
Yes	19	22.9			

N/A: Not applicable, SD: Standard deviation

RESULTS

Sociodemographic and Clinical Properties

A total of 83 patients with MDD (60 women and 23 men) and 85 healthy controls (49 women and 36 men) completed the study. The mean age for the patient group was 34.01±12.41 years and for the control group 34.21±12.1years. The two groups were compared with regard to age, gender, education, occupation, socioeconomic class, and status of smoking. As shown in Table 1, patients and controls did not differ significantly in any of these features.

The duration of illness was 5.09±4.06 years. The average age at the first depressive episode experienced

by the subjects was 28.91±9.6 years. The mean number of depressive episodes was 3.25±0.81. Among the patients, 31.3% (n=26) had made at least 1 suicide attempt. Mean and SD for BDI, BAI and BHS scores were 16.37±10.69; 16.84±7.17, and 8.20±4.22 for the patient sample, respectively.

Empathy and Associated Clinical and Sociodemographic Features

PT, EC, and FS empathy subscores were all substantially lower in subjects with depression than in healthy controls, while the PD empathy subscore was higher than in healthy subjects, as shown in Table 2. We then investigated the role of gender in the scores of the empathy subscales. We conducted GLM analyses with age and education as continuous predictors and gender and diagnosis as categorical predictors, and PT, EC, FS, and PD subscores of IRI as dependent variables. Gender significantly contributed to scores on the EC and FS scales. Female participants scored significantly higher on these scales (EC: 22.60±3.90 versus 20.90±2.50, F=23.27; p<0.001 and FS: 15.82±4.90 versus 11.32±5.41, F=42.23; p<0.001, respectively). Age significantly contributed only to FS subscores after

statistically controlling for the main effects of the experimental group. Education did not contribute significantly to any empathy subscore (F=17.84, p<0.001 and F=1.486; p=0.07, respectively). There was an interaction between gender and group in the FS subscale. This interaction reflected increased EC and FS scores in subjects with female patients compared to male patients (F=9.065; p=0.003 and F=33.46; p<0.001, respectively).

We investigated effects of age and years of education as continuous predictor variables, gender, previous psychotic mood episode and previous suicide attempt as dichotomous categorical variables, on empathy subscores. The results, summarized in Table 3, showed that education did not significantly contribute to any empathy score while age significantly contributed to FS scores in this model (F=29.69, p<0.001). Previous suicidal attempt significantly related only to EC scores. The EC score was significantly lower in subjects with depression who had made suicide attempts than in those who had not (F=6.75, p=0.014; 24.10±3.50 versus 20.30±6.30). The interaction between suicidal attempt and gender did not significantly contribute to any empathy score. In addition, both previous psychotic mood episode and the interaction between suicide and

Table 2: IRI scores in subjects with major depressive disorder in comparison with healthy subjects

	Major Depressive Disorder (n=83)		Healthy Controls (n=85)		F	p	Effect size (partial eta-squared)
	Mean	SD	Mean	SD			
IRI-Perspective Taking (PT)	17.19	6.30	20.85	2.63	25.4	<0.001*	0.136
IRI-Fantasy Scale (FS)	22.00	4.44	22.41	2.29	6.01	0.015*	0.036
IRI-Empathic Concern (EC)	14.98	8.10	15.06	2.64	9.34	0.003*	0.054
IRI-Personal Distress (PD)	17.04	7.81	11.28	2.82	27.7	<0.001*	0.146

*Statistically significant, IRI: Interpersonal Reactivity Index, SD: Standard deviation

Table 3: Relationships between the IRI scores and clinical features in subjects with major depressive disorder

	IRI-PT	IRI-EC	IRI-FS	IRI-PD
Current Age	2.577 (0.113)	0.520 (0.473)	29.690 (<0.001)*	0.086 (0.770)
Gender	0.483 (0.489)	8.734 (0.004)*	9.126 (0.003)*	0.274 (0.602)
Length of education	1.432 (0.235)	0.313 (0.577)	1.224 (0.187)	1.326 (0.254)
Previous suicide attempt	0.099 (0.754)	6.750 (0.014)*	0.001 (0.978)	3.854 (0.053)
Psychotic mood episode	0.904 (0.345)	1.281 (0.261)	0.004 (0.947)	0.264 (0.609)
Previous suicide attempt X previous psychotic mood episode	1.306 (0.257)	2.015 (0.160)	1.637 (0.205)	2.343 (0.130)

Table shows F ratios from general linear model analysis; df= 1. Current age and years of education were continuous variables; suicide history, previous psychotic mood episode and gender were dichotomous categorical predictor variables; and the Interpersonal Reactivity Index (IRI) scores were dependent variables. P values of F ratios are in parentheses. *Statisticaly significant

Table 4: Pearson's correlations of numeric clinical variables with empathy scores in major depressive patients

	IRI-PT	IRI-EC	IRI-FS	IRI-PD
Age at illness onset	0.132	-0.098	-0.533**	0.064
Duration of illness	-0.177	-0.533**	-0.842**	-0.492**
Number of hospitalizations	0.124	0.16	0.105	0.174
Number of depressive episodes	-0.119	-0.231	-0.533**	-0.469**
Number of suicide attempts	-0.288	-0.165	-0.039	-0.083
Scales				
Beck Hopelessness Scale (BHS)	-0.141	-0.414**	-0.333**	-0.179
Feelings of future	-0.006	-0.218*	-0.499**	-0.278*
Loss of motivation	0.071	0.162	-0.096	0.019
Expectations	-0.411**	-0.339**	-0.344**	-0.094
Beck Depression Inventory (BDI)	0.041	-0.087	-0.176	-0.181
Beck Anxiety Inventory (BAI)	0.076	-0.041	-0.168	0.235*

*<0.05, **<0.001, IRI: Interpersonal Reactivity Index

Table 5: Comparison of IRI scores in major depressive patients with high risk and low risk of suicide

	High risk of suicide (n=31)		Low risk of suicide (n=52)		F	p	Effect size (partial eta-squared)
	Mean	SD	Mean	SD			
IRI-Perspective Taking (PT)	16.94	3.72	17.35	7.46	1.674	0.20	0.02
IRI-Fantasy Scale (FS)	20.90	4.56	22.65	4.28	2.992	0.09	0.04
IRI-Empathic Concern (EC)	10.22	4.72	17.81	8.40	36.839	<0.001	0.32
IRI-Personal Distress (PD)	12.90	5.84	19.50	7.84	14.182	<0.001	0.16

Results have been controlled for sex, age, Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI) scores in MANCOVA test, SD=standard deviation, IRI: Interpersonal Reactivity Index

psychotic mood episode did not significantly contribute to any empathy score (Table 3).

We found a significant negative correlation between the number of depressive episodes and the scores on the FS and PD subscales (r=-0.533, p<0.001 and r=0.469, p<0.001, respectively). All empathy subscores had no correlation with BDI in subjects with MDD, whereas BAI was significantly correlated with the scores of the PD subscales (r=0.235, p<0.05). There were significant negative correlations between BHS and FS and EC scores (r=-0.333, p<0.05 and r=-0.414, p<0.001). Age at illness onset significantly and negatively correlated with FS scores (r=-0.533, p<0.001). We found significant negative correlations between duration of illness and EC, FS, and PD scores (r=-0.533, p<0.001; r=-0.842, p<0.001 and r=-0.492, p<0.001, respectively) (Table 4).

According to the cutoff point of 9 in the total score of the BHS, 37.3% (n=31) of the patients were classified as being at high risk of suicide and 62.7% (n=52) as low risk. We used a multivariate analysis of covariance test to compare IRI scores of patients with high risk and low risk of suicide. According to this test, FS and PD empathy subscores were substantially lower in subjects with high risk of suicide group than in the low risk group even after adjusting for sex, age, and psychopathological severity, as shown in Table 5 (F=36.83 p<0.001 and F=14.18, p<0.001, respectively).

DISCUSSION

The present study mainly demonstrated a significant impairment in both affective and cognitive empathy in depression. With respect to affective empathy, some studies reported that patients with MDD showed a significantly higher level of PD compared to controls (12,30,31). Batson et al. (4) hypothesized that the emotional pain associated with empathic distress may cause depressed individuals to show less EC. There is only one study reporting decreased EC scores in patients compared to controls. This result was supported by the current findings and may indicate that

low EC reflects an increase in preoccupation with the self and negative ruminations often observed in persons with depression (32,33). In a review study, Schreiter et al. (34) suggested that a high level of self-focus, which is common in depression, may help explain findings of high PD and low EC in this state. On the other hand, O'Connor et al. (12) reported elevated levels of PD, but no reduction in EC, in response to others' concerns in acutely ill patients with MDD. We did not find any relationship between depression severity and EC scores. We also observed a significant negative correlation between duration of illness and EC scores. Therefore, this finding may suggest the possibility that impaired EC may be a consequence of repeated episodes of illness or the sequel of the disease process rather than an illness state.

Another important result of this study was that depressive subjects had lower PT and FS scores than healthy controls. The current finding is consistent with previous studies of impairments in PT in patients with MDD (35-37). One explanation for this finding is that depressed individuals have difficulties letting go of an egocentric attitude in order to affirm the perspective of another person (38,39). Otherwise, impaired perspective-taking ability may be related to impairment in cognitive processes which were reported in patients with MDD (40-43). Theoretically, the absence of a correlation between PT scores and illness burden indicates the possible presence of a deficit in PT from the beginning of the disorder. In this view, low PT could become one of the risk factors that precede the onset of MDD. Also, in the present study FS was found to be inversely related with illness burden. This finding may be interpreted to mean that lower FS may facilitate the chronicity of MDD. The connection between neuroticism and FS may support this hypothesis, because patients with high scores in neuroticism are likely to suffer from more chronic episodes of depression (44,45). In this context, our finding indicates that pharmacological or psychosocial interventions improving interepisodic empathic ability may improve prognosis in depressive patients with these features; this should be confirmed by longitudinal and intervention studies. Practical implications that emerge from these findings would

imply the need for developing prevention programs targeted at improving cognitive empathic ability as a trait feature in these patients.

The relationship between suicide and psychiatric disorders is an important area. Yet, a single risk factor is not sufficient to predict suicide. As Pompili et al. (46) wrote: "Despite intensive efforts, effective prediction and prevention strategies have remained elusive". To date, there have been no studies examining the relation between empathic responding and suicidality in patients with MDD. Our study indicates that the impairment in empathic ability may be associated with suicidality in these patients. Our findings demonstrate that depressive subjects with a previous suicide attempt had lower EC scores than those without, and the EC score was also not related to current suicidal intent in the present study. However, a low PD score was found to be related to a high risk of suicide. Thus, it could be assumed that suicide attempts in depressed patients are partly facilitated by the impairment in affective empathy. PD and EC scores were found to be related with social and behavioral sensitivity (2,25). Because these other-oriented traits contribute to prosociality and therefore lead to positive outcomes during social interaction, an impairment in these traits could make depressive patients more vulnerable to attempting suicide. Therefore, it is important to note that there is a need to develop specific interventions which would be focused on the association between suicide and empathy in recovered depressed patients. On the other hand, it is reasonable to suggest that impairment in EC ability in suicidal patients might have biological implications in MDD (47-49).

In the present study, FS scores significantly and negatively correlated with BHS total and feelings about future subscores, and a lower FS score was associated with high suicide intent. Lee et al. (44) reported that FS acted as a partial mediator in the neuroticism-depression connection. Neuroticism predicts the onset of depressive disorders and is closely related to hopelessness and suicidality (45). In this regard, neuroticism may be a factor underlying the inverse relationship between suicidality and FS reported by the current study. From a theoretical viewpoint, our

findings indicate that interventions increasing the fantasy ability may decrease suicidality in major depression, which may be confirmed by longitudinal and intervention studies. Yet, one must exercise some caution while interpreting these results, because to our knowledge, no other studies have investigated the relationship between suicidality, hopelessness, and empathy in major depression.

In the present study, we observed significant gender differences in empathy scores, with female participants scoring significantly higher on EC and FS scales. Women have long been considered more empathetic than men (4,5). Compared to men, women are more likely to have higher scores on PD and EC, while gender differences on PT and FS scores have not been observed (14,15). Our findings partially confirmed previous findings of high scores on EC in female participants. However, the relation between empathy, depression, and gender is still unclear. Few studies indicate that depressed women are more likely than depressed men to be impaired in empathic ability (50,51). On the contrary, we found that female patients scored higher on the FS subscale than male patients. This may be explained by the fact that the FS subscale represents a cognitive empathic responding to an imagined, not a real, condition. The higher FS scores may indicate that females with depression may be more sensitive to imagined than to real stressful conditions compared to men. Also, this new finding may be associated with differences in verbal intelligence and neuroticism between the two genders, which were reported to be closely related to FS scores (13,44). Therefore, the current findings could open up a new area for studies examining gender differences in major depression. Moreover, clinicians must consider gender differences in empathic ability in their patients when treating major depressive disorder.

Some limitations of the present study must be considered. As with most studies on patients with depression, all patients were on antidepressant medication, which may affect empathy and cognitive ability measures. Thus, it is important to note that our results could be affected by the antidepressant use. No one in our patient group had any other psychiatric comorbidity, and the sample may not be representative of the clinical population. An obvious drawback of the IRI, BHS, BAI, and BDI data is that they are based on self-report. This is a cross-sectional study of baseline parameters; hence the longer-term associations between empathy and clinical properties were not addressed. In addition, it could be interesting and valuable to investigate the relationship between symptomatology and empathy in depressed patients. Finally, we did not consider cognitive functioning, which may also play a crucial role in the relationship between empathic abilities and depression.

In conclusion, based on our results, patients with MDD show significantly impaired cognitive and affective empathy measures compared to the normal population, and patients with different clinical characteristics may show different empathic responding patterns. Our findings also suggest a close relationship between suicidality and empathy in patients with MDD. In addition, the current study indicates significant gender differences in empathic ability in depressive patients. However, a prospective study of empathic skills in a larger sample is required to explore how empathic responding changes with clinical variables. Finally, future studies using neuroimaging methods to examine the neural substrates of empathic abilities in MDD will provide a significant contribution to the putative biological causes underlying complex relationships between gender, suicidality and empathy in this illness.

Contribution Categories	Name of Author
Development of study idea	O.E., A.E.
Methodological design of the study	O.E., A.E.
Data acquisition and process	O.E., A.E.
Data analysis and interpretation	O.E.
Literature review	O.E., A.E.
Manuscript writing	O.E., A.E.
Manuscript review and revisation	O.E.

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