Pre-morbid alexithymia in panic disorder: A cohort study

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ABSTRACT

Whether alexithymia is a personality trait which increases the risk of Panic Disorder (PD) is still debated. In this prospective study, alexithymic levels were evaluated before, during and after an anxious episode. Therefore, the alexithymic levels, the presence of PD and the severity of anxious-depressive symptoms were evaluated, at intervals of about 1 month, in pregnant women, attending the Centers for Prenatal Care, using the Toronto Alexithymia Scale (TAS-20), the Primary Care Evaluation of Mental Disorders and the Hospital Anxiety and Depression Scale (HADS). Twenty-one women affected by PD and 256 healthy women (controls) were included in the study. Women who developed PD, compared to controls, showed similar TAS-20 and HADS scores during the pre-morbid phase, a significant increase of them during PD and a significant decrease after symptoms improvement, whereas no change was observed in controls. Our data suggest that in pregnant women alexithymia does not represent a personality trait that increases the risk of developing PD, and they support the hypothesis that alexithymia is a state dependent phenomenon in PD pregnant women.

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1. Introduction

A personality characterized by difficulty to process or regulate emotions using cognitive strategies (alexithymia) is supposed to increase the risk for mental disorders such as major depression (Celikel et al., 2010), panic disorder (Marchesi et al., 2005), eating disorders (Carano et al., 2006) and substances abuse (de Timary et al., 2008).

Concerning Panic Disorder (PD), high rates of alexithymia have been found in PD patients (Parker et al., 1993; Zeitlin and McNally, 1993; Cox et al., 1995; Bankier et al., 2001; Iancu et al., 2001; Marchesi et al., 2000, 2005). This finding was explained by different hypotheses: (1) alexithymia, as a personality trait, precedes and predisposes people to PD (Parker and Taylor, 1997); (2) alexithymia is nothing more than a state reaction (secondary alexithymia), which mitigates painful affects in patients with a mental disorder (Freyberger, 1977; Ahrens and Deffner, 1986; Wise et al., 1990) and (3) the large proportion of PD patients reporting high TAS-20 score should not be considered alexithymic because a conceptual and psychometric overlap may exist between alexithymia and cognitive aspects of PD (Cox et al., 1995; Marchesi et al., 2005).

This controversy might be resolved with longitudinal studies by evaluating alexithymia in PD patients before and after remission. At present, we have knowledge of only three longitudinal studies (Fukunishi et al., 1997; Marchesi et al., 2005; Rufer et al., 2010). In the first and the second study (Fukunishi et al., 1997; Marchesi et al., 2005) the TAS-20 score decreased after treatment and the decrease was significantly related to reduction of anxiety, suggesting that alexithymia should be considered a state reaction. In the third study (Rufer et al., 2010), similar results were found, whereas the authors' conclusions were somewhat different since they claim that alexithymia is a "complex manifestation that includes both trait and state components".

These longitudinal studies questioned the absolute stability of alexithymia, which implies that no significant changes should be observed over time, and they suggested that alexithymia is characterized by a state component. However, some authors (Luminet et al., 2001; Taylor and Bagby, 2004; Saarijärvi et al., 2006; Lumley et al., 2007) claim that the reduction of alexithymic levels with the improvement of symptoms severity should not be considered a finding against the trait hypothesis, since if the relative differences in alexithymic scores remain the same among patients (relative stability) the trait hypothesis is confirmed. Therefore, the relative stability is supposed to be a characteristic of alexithymia as personality trait in their view. Nevertheless, the relative stability does not provide any information regarding the pre-morbid alexithymic levels in PD patients and then it cannot represent a conclusive finding supporting the trait hypothesis. This conclusion was also stated by Mikolajczak and Luminet (2006).

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(two authors supporting the trait hypothesis), who claimed that “the stability of alexithymia scores at follow-up would not constitute evidence that alexithymia preceded mental disorder”.

In our knowledge no studies have investigated alexithymia in a premorbid phase of PD.

Therefore, the present study was aimed to verify how alexithymic levels were before, during and after a PD episode. For this purpose we evaluated alexithymia and the presence of an episode of PD in a sample of women, attending the Centers for Prenatal Care, at approximately monthly intervals during the whole pregnancy.

2. Methods

The study protocol was approved by the Local Ethical Committee.

2.1. Sample

The study population was recruited among women who consecutively sought assistance at the Centers for Prenatal Care of the Public Health Service of District of Mantova (Italy), from September 2005, and Reggio Emilia (Italy), from January 2007.

Women participated in the study after the procedure had been fully explained and a written informed consent was obtained, if they were older than 18 years and completed all the evaluations from the beginning of their pregnancy.

The study included 299 women. Twenty-two women were excluded from the study because they presented during pregnancy anxious symptoms, which did not satisfy the diagnostic criteria of PD: the criteria of Generalized Anxiety Disorder (GAD) were satisfied in six women and those of anxiety disorder not otherwise specified (NOS) in 16. These women were excluded from the study because it was aimed to evaluate alexithymia before, during and after the episodic manifestations of an anxiety disorder, and PD seems the only disorders, diagnosed with the PRIME-MD (PD, GAD and anxiety disorder NOS)(see assessment), which presents this characteristic.

Therefore the study population included 277 women: 21 were diagnosed as affected by PD and the remaining 256 did not present anxious symptoms during pregnancy (healthy controls)(C).

2.2. Assessment

At each visit, all women were asked to complete (approximately every month) the following evaluations: (1) the Italian translation of the Primary Care Evaluation of Mental Disorders (PRIME-MD) (Spitzer et al., 1994), for the screening of PD; (2) the Italian translation of the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983) for the evaluation of severity of anxious and depressive symptoms and (3) the Italian version of the TAS-20 (Bressi et al., 1996), for the assessment of alexithymic levels.

Moreover, all women completed a brief questionnaire, performed *ad hoc*, to collect socio-demographic and anamnesis information.

The PRIME-MD is a structured interview for the diagnosis of mental disorders according to the criteria of DSM-IV (American Psychiatric Association, 1994), and was administered at each visit by the gynecologists, who were trained by a senior psychiatrist. Three anxiety disorders can be diagnosed with the PRIME-MD: PD, GAD and anxiety disorder NOS.

A woman was defined as affected by PD if, at any evaluation during pregnancy, she fulfilled the criteria for a PD episode. A woman was defined as healthy control if she did not present any anxious symptoms at any evaluation during pregnancy.

The TAS-20 is the most widely used measure of the alexithymia construct. It is a self-rated questionnaire, composed by 20 items that are rated on a five-point Likert scale. The items load on three factors: Difficult in Identifying Feeling (DIF), Difficult in Describing Feeling (DDF) and Externally Oriented Thinking (EOT).

The HADS is a self-administered instrument for the evaluation of anxiety and depression in a non-psychiatric population. The seven items of the depression subscale were largely based on the anhedonic state: in fact, five items are related to the loss of pleasure. The seven items of the anxiety subscale were chosen from the psychic manifestations of anxiety. Therefore, HADS generates two subscale scores: the anxiety score and the depression score.

2.3. Statistical analysis

Comparisons between PD and C women were performed using the two-tailed Student *t*-test, for continuous variables and with the χ^2 test for categorical variables.

One-way analysis of variance for repeated measures was used to evaluate whether TAS-20 and HADS subscales scores changed during pregnancy in C and in PD women.

Two-tailed Student *t*-test was used to compare TAS-20 and HADS subscale scores in the two groups of women. Three comparisons of TAS-20 and HADS subscales scores were performed between PD and C women. The evaluations before, during and after the acute anxious episode were used for PD women. When more than one evaluation was available before or after the anxious episode, we used the evaluation corresponding to the lowest severity of anxious symptoms, whereas if more than one evaluation was available during PD we used that corresponding to the highest severity of anxiety symptoms. For C women we used the evaluations corresponding to the same time of those of PD women, because they did not show any significant change in TAS-20 and HADS subscales scores during pregnancy (see results).

To test the relative stability of alexithymia in PD women, a stepwise linear regression analysis (forward selection) was used: in the analysis, TAS-20 total scores after anxious symptoms improvement were used as dependent variable and TAS-20 total scores before and during PD and HADS subscale scores after anxious symptoms improvement were used as independent variables.

An analysis of covariance was used to evaluate whether the difference in TAS-20 scores (dependent variable) between PD women during the anxious phase and C women (independent variable) were still present after controlling for the HADS subscale scores (covariates).

Finally, logistic regression (enter method) was used to test whether the TAS-20 scores at the beginning of pregnancy (used as independent variable) predicted the development of PD during pregnancy (presence or absence of PD was used as dependent variable).

3. Results

3.1. Sample

The study included 299 women with a mean age of 30.7 ± 4.4 years (18–45 years). Twenty-two women were excluded from the study because they presented during pregnancy anxious symptoms, which did not satisfy the diagnostic criteria of PD (GAD or anxiety disorder not otherwise specified). Therefore the study population included 277 women: 21 were diagnosed as affected by PD and the remaining 256 were did not present anxious symptoms during pregnancy (C). PD and C women showed the same age, years of education and family or occupational status (Table 1).

The PD symptoms became evident after 4.0 ± 2.1 months of pregnancy and they lasted for 3.0 ± 2 months (Table 1).

Table 1
Socio-demographic and clinical features in pregnant women who developed panic disorder, and in healthy pregnant women.

	Panic disorder	No anxiety		
	<i>n.</i> 21	<i>n.</i> 256		
Age (years)(mean $\pm$ S.D.)	31.9 $\pm$ 3.9	30.7 $\pm$ 4.4	<i>t</i> = 1.2	<i>p</i> = 0.23
Education (years) (mean $\pm$ S.D.)	11.0 $\pm$ 3.1	12.3 $\pm$ 3.3	<i>t</i> = 1.7	<i>p</i> = 0.08
Family status			χ^2 = 4.7	<i>p</i> = 0.58
Never married	2 (9.5%)	41 (16.0%)		
Married	18 (85.7%)	186 (72.7%)		
Living together	1 (4.8%)	27 (10.5%)		
Separated/divorced	–	2 (0.8%)		
Occupation			χ^2 = 4.3	<i>p</i> = 0.21
Unemployed	0	1 (0.8%)		
Student	0	2 (1.7%)		
Housewife	6 (37.5%)	8 (7.1%)		
Employed	10 (62.5%)	101 (90.1%)		
Number of assessments				
Total (mean $\pm$ S.D.)	6.1 $\pm$ 1.3	6.0 $\pm$ 1.3	<i>t</i> = 0.43	<i>p</i> = 0.66
Before PD	2.9 $\pm$ 2.9	–		
After PD	2.2 $\pm$ 2.2	–		
Anxious episode (mean $\pm$ S.D.)				
Time of onset (months)	4.0 $\pm$ 2.1	–		
Duration (months)	3.0 $\pm$ 1.2	–		

3.2. Treatment

None of the PD women received a pharmacological treatment and only three women were treated with cognitive-behaviour therapy because the severity of anxious symptoms. However, at each visit, PD women received a psychological support given only in non-standardized manner and they were encouraged to expose themselves to the threatening situations.

3.3. Assessment

The number of assessments was similar in PD and in C women (Table 1).

3.3.1. Alexithymia and symptom severity

The TAS-20 and the HADS subscales scores in PD women (before, during and after the anxious episode) and in controls are presented in Table 2. C did not show any change in the TAS-20 and HADS subscale scores across all evaluations, whereas, in women who developed PD symptoms the pre-morbid TAS-20 and HADS scores were similar to those observed in C women, they significantly increased during the acute phase of PD and decreased after symptoms improvement (Table 2).

Logistic regression analysis showed that TAS-20 score at the beginning of pregnancy did not predict the development of PD during pregnancy (wald=0.01; $p=0.98$; OR=1.00; CI 95%=0.94–1.06).

In PD women, linear regression analysis showed that the TAS-20 total scores after symptoms improvement were positively related to the alexithymic levels observed during acute PD phase ($b=0.54$; $t=6.6$; $p<0.001$), but not to pre-morbid levels ($b=0.04$; $t=0.5$; $p=0.56$), controlling the effect of symptom severity after improvement (HADS-A: $b=0.14$; $t=1.9$; $p=0.05$).

Finally, the differences in TAS-20 score observed between PD women, both during illness phase and symptoms improvement, and C disappeared after controlling for the severity of anxiety and depressive symptoms (ANCOVA: $F=1.34$; d.f.=1,273; $p=0.24$ and $F=0.22$; d.f.=1,273; $p=0.63$, respectively).

4. Discussion

To our knowledge, this is the first prospective study investigating pre-morbid alexithymic levels in women with an episode of PD.

In C women alexithymic levels did not change during the whole pregnancy. In contrast, in PD women during the pre-morbid period the alexithymic levels were similar to those of women who maintained a healthy condition and, at the beginning of pregnancy, the TAS-20 scores did not predict the development of PD. Moreover, in PD women alexithymic levels significantly increased during the acute phase of illness and significantly decreased after symptoms improvement (even though higher levels were still present). Finally, in PD women after symptoms improvement, alexithymic levels were positively related to the TAS-20 scores during PD (but not to pre-morbid scores) and to the severity of residual anxiety symptoms.

All together our data suggest that in pregnant women alexithymia does not represent a personality trait that increases the risk to develop PD episode, and they support the hypothesis that alexithymia is a state dependent phenomenon. According to the state-hypothesis, in our study alexithymia levels were in the normal range before the PD onset, increased as anxiety became clinically relevant and decreased after the improvement of symptoms.

Some authors (Taylor and Bagby, 2004; Lumley et al., 2007; Rufer et al., 2010) suggest that alexithymia, as a personality trait, is characterized by relative stability: even though the alexithymic levels can decrease from the acute to the remission phase, the relative differences among individuals remain stable over time. This hypothesis implies that the basic personality conditions, which constitute a predispositional factor to an anxiety disorder, are accentuated by the state of illness and return to the pre-existing conditions after remission, as suggested by Hoffart (1994) in his predisposition-state model. However, to our knowledge no previous study has demonstrated that the alexithymic levels observed in the remitted state corresponded to those of the pre-morbid phase.

Also in our study alexithymia showed a relative stability; however, our data demonstrated that TAS-20 score assessed after improvement of PD symptoms did not represent a return to the

Table 2

TAS-20 and HADS scores in women who developed Panic Disorder (PD) during pregnancy and in healthy pregnant women (C).

Scores	mean $\pm$ S.D.			T ₁ vs. T ₂ vs. T ₃		PD vs. C			
	T ₁	T ₂	T ₃	One-way ANOVA for repeated measures		t-test d.f.=275			
TAS-20				F	p		T ₁	T ₂	T ₃
PD (n. 21)	36.7 $\pm$ 10.1	62.1 $\pm$ 9.0	45.3 $\pm$ 13.2	7.7	0.009	t	1.0	9.5	4.3
C (n. 256)	34.5 $\pm$ 9.0	37.2 $\pm$ 11.8	35.2 $\pm$ 9.9	0.8	0.44	p	0.29	< 0.001	< 0.001
DIF									
PD	11.6 $\pm$ 4.1	21.2 $\pm$ 6.9	14.4 $\pm$ 6.3	5.5	0.03	t	0.7	6.2	2.3
C	10.6 $\pm$ 4.9	11.2 $\pm$ 5.4	10.7 $\pm$ 4.3	0.4	0.62	p	0.45	< 0.001	0.02
DCF									
PD	9.6 $\pm$ 4.3	15.1 $\pm$ 5.4	9.2 $\pm$ 4.6	4.1	0.04	t	0.3	4.4	0.1
C	9.2 $\pm$ 3.5	9.6 $\pm$ 4.1	9.1 $\pm$ 3.8	0.9	0.40	p	0.73	< 0.001	0.92
EOT									
PD	15.5 $\pm$ 4.9	22.2 $\pm$ 4.4	16.2 $\pm$ 4.4	10.2	0.004	t	6	3.7	0.42
C	16.6 $\pm$ 5.1	16.8 $\pm$ 5.1	17.3 $\pm$ 5.4	0.2	0.81	p	0.49	< 0.001	0.66
HADS-A									
PD	3.8 $\pm$ 3.4	11.2 $\pm$ 3.0	6.8 $\pm$ 3.0	9.3	0.003	t	0.6	9.9	3.2
C	3.2 $\pm$ 2.5	3.3 $\pm$ 2.7	3.1 $\pm$ 2.5	0.3	0.73	p	0.53	< 0.001	0.002
HADS-D									
PD	3.2 $\pm$ 1.7	6.8 $\pm$ 2.6	4.6 $\pm$ 2.8	8.2	0.007	t	0.7	8.4	3.3
C	2.8 $\pm$ 2.8	2.9 $\pm$ 2.5	2.7 $\pm$ 2.6	0.4	0.68	p	0.48	< 0.001	0.002

HADS-A: anxiety subscale score, **HADS-D:** depression subscale score, **T₁:** before the onset of anxiety episode in PD women, **T₂:** during anxiety episode in PD women, **T₃:** after symptoms improvement in PD women, In C women **T₁**, **T₂** and **T₃** represent the evaluations assessed at the same time of those of women with PD.

pre-morbid conditions, because at this time a residual anxiety symptoms can maintain an elevation of alexithymic levels, as suggested by a positive relationship between HADS-A and TAS-20 scores after symptoms improvement. Therefore, our study suggests that in patients affected by PD the alexithymic reaction might resolve only after many months of remission, when also residual symptoms disappeared and symptom severity returned to the pre-morbid level. Otherwise, the presence of residual anxiety symptoms seems a sufficient condition to prevent the normalization of the alexithymic reaction.

Therefore, our data do not confirm that relative stability is a finding supporting the hypothesis of alexithymia as a personality trait, and they suggest that relative stability of alexithymia in PD patients is the results of a parallel change between symptoms severity and alexithymic scores, which wax and wane together. The hypothesis that alexithymic levels were modulated by the severity of symptoms is also supported by the disappearance of the differences in TAS-20 scores observed between PD women during the illness phase and in partial remission phase and C women after controlling for symptom severity. Therefore, our data confirm both the suggestion of Hoffart (1994), who claimed that to support the hypothesis that a personality feature constitutes a predispositional factor to one disorder, the personality differences observed between diagnostic groups should persist after symptom severity has been controlled for, and that of Lumley (2000), who stated that the uniqueness of the TAS-20 in the relationship with anxiety could be tested by statistically controlling the other construct and examining the residual relationship of the TAS-20 with the criterion.

There are at least two alternative explanations for the relationship between alexithymia and PD observed in our study. Alexithymia may be a temporary response to stress represented by a PD episode; in this view “secondary alexithymia” can represent a defense or a strategy to cope with distress (emotional pain and physiological arousal) associated with PD (Lumley, 2000). In the second view, the relationship between alexithymia and PD may represent an artefact of the method and measures used (Lumley, 2000). Particularly, the TAS-20 dimensions “difficult identifying feelings” and “difficulty describing and communicating feelings” correlate with different measures of negative affects (Cox et al., 1995; Berthoz et al., 1999; Lumley, 2000; Marchesi et al., 2000; Hintikka et al., 2001; Honkalampi et al., 2001). Therefore people with negative emotional states (i.e. anxiety and depression) may score high on these TAS-20 dimensions.

The present study does not allow any conclusion regarding which view represents a better explanation of our results, because our data may support both these hypotheses.

However, some methodological aspects limit the generalization of our results.

First of all, given the small sample size of our PD women, firm conclusions should be drawn from our results with precaution and the present data need to be verified by using larger samples and longer follow-up periods. Nevertheless the presence of PD symptoms, their severity and alexithymic features were frequently and carefully monitored in our sample.

Second, we measured alexithymia only by a mean of a self-rated questionnaire (TAS-20). This evaluation should be affected, on the one hand, by the hampered ability of introspection, which might characterized alexithymic people, and, on the other hand, by the maintained ability of these subjects to recognize and report in an undifferentiated manner negative affect on a questionnaire, whose score is highly correlated with anxiety, depression or neuroticism.

Third, we studied alexithymia and PD in a particular setting, represented by pregnant women; therefore one can assume that our data can be poorly generalized to other PD patients. However,

no study has demonstrated that PD symptomatology occurring in pregnancy is different to that occurring in other conditions. Nevertheless, in our sample only a minority of women showed during pregnancy a PD severe enough to need a treatment: in fact only 14% of women received a cognitive-behaviour therapy. Therefore, our data can be generalized to subjects affected by mild-moderate PD.

Fourth, PD was not diagnosed by a psychiatrist and therefore our data might be poorly reliable.

However, the PD was diagnosed using the PRIME-MD, an interview performed to evaluated mental disorders in primary care, which showed a good reliability between diagnoses obtained by trained physicians and those obtained by psychiatrists (Spitzer et al., 1994). Moreover, the PRIME-MD showed good specificity (99%) and sensitivity (57%) in detecting PD in primary care (Spitzer et al., 1994).

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