



## 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  $\chi^2$  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  $30.7 \pm 4.4$  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  $4.0 \pm 2.1$  months of pregnancy and they lasted for  $3.0 \pm 2$  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			$\chi^2$ = 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			$\chi^2$ = 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	–		

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