

## Pre-symptomatic testing for neurodegenerative disorders: Middle- to long-term psychopathological impact

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### Abstract

**Background:** Over the past 20 years, studies have revealed that the communication of a pre-symptomatic test (PST) result for late-onset diseases, such as Huntington's disease (HD), doesn't cause psychological disturbance. This cross-sectional study investigated the middle- (4 years) to long-term (7 and 10 years) psychological impact of PST for 3 autosomal dominant late-onset diseases: HD, Machado-Joseph disease (DMJ) and familial amyloid polyneuropathy (FAP). **Method:** The study included 203 subjects: 170 (84%) agreed to make the PST for FAP, 29 (14%) for HD and 4 (2%) for MJD. They were mostly women (58%) and married (67%). It was considered the cutoffs points: 4 years (middle-term) and 7 and 10 years (long-term) indicating the time after receiving the TPS results. **Results:** women and widows (oldest) presented the highest mean values for almost all BSI dimensions and the highest values correspond to the obsessive-compulsive dimension. MJD participants presented the highest mean values. No differences were found concerning the PST test results while participants are still asymptomatic. Psychopathology was only present in symptomatic carriers. **Conclusions:** The onset of the disease seems to assume the trigger for psychological disturbance, regardless the time that has elapsed since the PST result communication or the individual carrier/non-carrier condition.

**Keywords:** Pre-symptomatic testing, psychological impact, late-onset genetic diseases.

### Resumen

**Pruebas pre-sintomáticas de enfermedades neurodegenerativas: el impacto psicopatológico a largo plazo. Antecedentes:** el presente estudio transversal investigó el impacto psicopatológico a medio (4 años) y a largo plazo (7 y 10 años) de la prueba pre-sintomática (PPS) para tres enfermedades autosómicas dominantes de aparición tardía: enfermedad de Huntington EH, la enfermedad de Machado-Joseph (EMJ) y la polineuropatía amiloide familiar (PAF). **Método:** participaron 203 sujetos: 170 (84 %) realizaron el PPS para PAF, 29 (14 %) para EH y 4 (2 %) para EMJ. La muestra, en su mayoría, estuvo compuesta por mujeres (58 %) y por personas casadas (67 %). Fueron considerados como puntos de corte los 4, 7 y 10 años después de haber recibido el resultado de la PPS. **Resultados:** las mujeres y los viudos presentan las medias más altas. Los participantes con EMJ presentaron las medias más elevadas. No se encontraron diferencias significativas en lo concerniente a los resultados de PPS. La perturbación psicológica fue escasamente observada en los sujetos portadores que ya evidenciaban síntomas. **Conclusiones:** la aparición de los primeros síntomas parece constituir el detonante para la existencia de perturbaciones psicológicas, independientemente del intervalo de tiempo sucedido desde la comunicación de los resultados de la PPS o de la condición genética (portador/no portador).

**Palabras clave:** prueba pre-sintomática, impacto psicopatológico, enfermedades genéticas de aparición tardía.

The predictive testing (PST) model for late-onset neurodegenerative diseases such as Huntington's disease (HD), a rare disorder with a prevalence of ~1-7 in 100,000 individuals of European ancestry (Ramos et al., 2015), has been implemented and adapted for other late-onset diseases around the world (Hawkins, Ho, & Hayden, 2011), namely, Machado-Joseph disease (MJD) and Familial Amyloidotic Polyneuropathy (FAP), two Portuguese monogenic, autosomal and dominant diseases (Sequeiros et al., 2006), with a severe neurodegenerative evolution and no effective cure. In Continental Portugal, MJD has a prevalence of 1: 100,000,

and is considered a rare disease, except for the area of the Tejo Valley (1: 1000) (Bettencourt & Lima, 2011); signs of cerebellar ataxia, progressive external ophthalmoplegia and pyramidal signs are reported (Coutinho, 1996; Sequeiros et al., 2006). Although Amyloidosis is very rare (less than 1 case in 100,000 people worldwide) it is more frequent in some countries such as Portugal, wherein the Val30Met mutation occurs in 1 in 1,000 people in areas of higher incidence like Póvoa Varzim/Vila do Conde, the most likely focus of origin of the disease (with 1/3 of total Portuguese patients). Sousa (1995) described a disease prevalence of 90.3/100,000 and an average age of onset of 33.5 years. For FAP, an abnormal amyloid protein (TTR) is deposited in various organs leading patients to experience progressive limitations (Saraiva, 1986).

There are several studies about the PST psychosocial short-term impact (one year) that did not demonstrate a severe negative impact (Lêdo, Leite, & Sequeiros, 2013; Lêdo, Paneque, Rocha, Leite,

& Sequeiros, 2013; Rolim et al., 2006; Tibben, 2007). However, there are few studies investigating the PST psychosocial impact in the mid- to long-term (Almqvist et al., 2003; Decruyenaere et al., 2003; Decruyenaere et al., 2004; Gargiulo et al., 2009; Gonzalez et al., 2012; Timman, Roos, Maat-Kievit, & Tibben, 2004).

At the Center for Predictive and Preventive Genetics (CGPP), Institute of Molecular and Cell Biology (IBMC), University of Porto (Portugal), a national reference model was developed for one year of genetic counseling protocol for individuals at-risk for HD, MJD and FAP (Rolim et al., 2006). Lêdo and colleagues (2013) studied the psychopathological impact on this population a year after the PST protocol and noticed that values decreased significantly one year after the implementation of the PST, regardless of the disease studied or the test result; however, for all Brief Symptom Inventory (BSI) dimensions and global indexes, significantly higher values were found than those of control groups. Therefore, it became a priority to study the mid- to long-term PST psychological impact as a result of communicating the genetic status to subjects that underwent the PST, and compare the results obtained with those of the few studies for HD (Decruyenaere et al., 2003; Decruyenaere et al., 2004; Gargiulo et al., 2009; Timman et al., 2004). The main aim of this research is to increase the knowledge about follow-up studies investigating the long-term consequences of PST, as suggested by Timman and colleagues (2004) so that the adjustment of psychological support for this population may be possible in the context of the Portuguese reality.

#### Method

This research is a descriptive cross-sectional study, resulting from the compilation of the medical records of the subjects who completed the one year PST protocol at CGPP (including the molecular study) and discovered their genetic status at least three years ago, for three autosomal dominant late-onset conditions: HD, MJD and FAP.

#### Participants

Fifty eight percent of subjects were female and the majority of the responses correspond to age ranging up to 30 years [21-77]. The majority of subjects had mainly professions involving some responsibilities (1<sup>st</sup> Graffar Index) and a high level of education. Most of the subjects underwent the PST for FAP (84%) and 37% were identified as carriers; of these, 15% had become symptomatic and 5% having had a liver transplant (Table 1).

Out of the 203 subjects, 32% had been informed about their genetic status 4 years ago (middle-term), 47% 7 years ago and 21% 10 years ago (the long-term). Concerning the three different cutoff points, data were similar to data observed in the total sample, with the exception of those subjects who completed the protocol 10 years ago, where the age increases (31-40 years) and, consequently, raising the number of pensioners. Those subjects, who underwent the PST protocol 7 years ago, present the highest mean age and many of them are already retired.

#### Instruments

The socio-demographic data - *gender, age, profession, and current marital status* - were collected from a questionnaire sent to all participants. The questionnaire sent to carriers also included the following questions (clinical variables) "*Current clinical*

*status*", "*Still without symptoms?*", and "*Had a significant change in your life in recent years?*". No clinical variables were included in the questionnaire to non-carriers.

The dependent variable *psychopathology* was assessed using the BSI (Derogatis, 1993) adapted for the Portuguese population by Canavarro (2007). This instrument is composed of 53 items, rated on a Likert scale of five grades (0 "rarely" to 4 "very often"), nine dimensions and three global indexes which express psychometric ratings of emotional distress: global severity index (GSI), positive symptoms total (PSTI) and positive symptom distress index (PSDI).

#### Procedure

This study was accepted by the IBMC ethics committee. Information about the researcher, the nature and objectives of the study and the principle of confidentiality was displayed when the subjects were originally registered in the PST protocol. Participants were contacted by mail in order to answer the questionnaire that included sociodemographic and clinical data and the BSI.

#### Data analysis

The statistical analysis was performed using the PASW Statistics Program, version 22.0. Descriptive [frequencies (*N*

Table 1  
Sample description

		Frequencies ( <i>N</i> = 203)	Percentage (100%)
Gender	Female	118	58.1
	Male	85	41.9
Age	≤ 30 years	88	43.3
	31 - 40 years	62	30.5
	41 - 50 years	20	9.9
	51 - 60 years	22	10.8
	61 - 70 years	8	3.9
	≥ 71 years	3	1.5
Marital Status	Single	53	26.6
	Married	132	66.5
	Divorced	10	5.0
	Widow	3	1.5
	Retired	40	19.7
Profession	Unemployed	19	9.4
	Student	15	7.4
	1 <sup>st</sup> Graffar Index	59	29.1
	2 <sup>nd</sup> Graffar Index	11	5.4
	3 <sup>rd</sup> Graffar Index	4	2.0
	4 <sup>th</sup> Graffar Index	22	10.8
Type of Disease	5 <sup>th</sup> Graffar Index	33	16.3
	HD	29	14.3
	MJD	4	2.0
PST Result	FAP	170	83.7
	Non-carrier	91	44.8
Clinical Status	Carrier	112	55.2
	Non-carrier	89	44.5
	Asymptomatic Carrier	73	36.5
	Symptomatic Carrier	29	14.5
	Liver Transplanted (FAP carriers)	9	4.5

Note: PST=Pre-symptomatic Testing

and *n*), mean (*M*) and standard deviation (*SD*)] and inferential [bi-variate statistical (ANOVA, chi-square test and bi-varying correlation)] analyses were carried out.

Results

BSI descriptive analysis

When considering the three cutoff points of 4, 7 and 10 years, mean and standard deviation were very similar to the ones relating to BSI scores (Table 2). For the three cutoff points,  $\alpha$  was similarly high, pointing to a good scale reliability. Comparisons of means were performed but no statistically significant differences were found.

Comparison between the BSI means regarding independent variables

Analyzing the mean values for the BSI variables, regarding socio-demographic and clinical variables, some statistically significant results were found:

Socio-demographic variables

*Gender variable.* Female presented higher mean values than men for the BSI total scores and for BSI *somatization, interpersonal sensitivity, depression* and *phobic anxiety* dimensions. The mean values for GSI and PSTI revealed statistically significant differences (Table 3).

*Age variable.* Significant results were found in the *obsessive-compulsive* dimension -  $F(5, 189) = 2.325, p = .045; \eta^2 = .058$  - and in the PSTI -  $F(5, 189) = 2.551, p = .029; \eta^2 = .066$  -, meaning that mean age and values increase in a similar direction. The exception occurred with older subjects that presented the lower averages for the same *obsessive-compulsive* dimension,  $M_{\leq 30} (n = 88) = 4.71; M_{31-40} (n = 62) = 5.71; M_{41-50} (n = 20) = 6.22; M_{51-60} (n = 22) = 7.00; M_{61-70} (n = 8) = 9.29; M_{\geq 71} (n = 3) = 4.33$ . The same trend is verified for the PSTI -  $M_{\leq 30} (n = 88) = 21.24; M_{31-40} (n = 62) = 22.37; M_{41-50} (n = 20) = 22.20; M_{51-60} (n = 22) = 23.73; M_{61-70} (n = 8) = 21.75; M_{\geq 71} (n = 3) = 13.67$ .

*Marital status variable.* Widows presented significantly lower mean values for almost all dimensions than single, married and divorced subjects; and divorced subjects the highest for all the BSI dimensions (Table 4).

Clinical variables

*Type of disease.* *Phobic anxiety* [ $F(2, 192) = 9.434, p = .000; \eta^2 = .091$ ], *psychoticism* [ $F(2, 192) = 3.958, p = .021; \eta^2 = .040$ ] and PSDI values [ $F(2, 192) = 5.170, p = .007; \eta^2 = .054$ ] presented significant differences. MJD subjects showed higher mean values than FAP and HD subjects, regarding *phobic anxiety* [ $M_{HD} (n = 29) = 1.15; M_{MJD} (n = 4) = 7.50; M_{FAP} (n = 170) = 1.70$ ], *psychoticism* [ $M_{HD} (n = 29) = 2.35; M_{MJD} (n = 4) = 6.75; M_{FAP} (n = 170) = 2.34$ ] and PSDI [ $M_{HD} (n = 29) = 1.47; M_{MJD} (n = 4) = 2.27; M_{FAP} (n = 170) = 1.44$ ].

*PST results variable.* Significant differences were found in *somatization* [ $F(1, 193) = 6.035, p = .015; \eta^2 = .029$ ] and PSDI [ $F(1, 193) = 4.569, p = .034; \eta^2 = .021$ ], where carriers (c) showed higher mean values than non-carriers (nc): *somatization*:  $M_c (n = 112) = 4.78$  and  $M_{nc} (n = 91) = 3.14$ ; PSDI:  $M_c (n = 112) = 1.52$  and  $M_{nc} (n = 91) = 1.37$ . *Current clinical status variable.* Statistical significant values were found in *somatization* [ $F(3, 189) = 7.451, p = .000; \eta^2 = .104$ ] and PSTI [ $F(3, 189) = 3.269, p = .023; \eta^2 = .048$ ]. Non-carriers [ $M (n = 89) = 3.14$ ] and asymptomatic carriers [ $M (n = 73) = 3.58$ ] had lower mean values than symptomatic carriers [ $M (n = 29) = 7.63$ ] and, in FAP disease, liver transplanted subjects [ $M (n = 9) = 5.43$ ]. For PSTI, non-carriers [ $M (n = 89) = 21.72$ ], asymptomatic carriers [ $M (n = 29) = 20.55$ ] and liver transplanted carriers [ $M (n = 9) = 17.44$ ] presented lower mean values than symptomatic carriers [ $M (n = 29) = 27.00$ ].

*“Still without symptoms?” variable.* In the carriers group, significant differences were found for all BSI dimensions and GSI, PSTI and PSDI, except for the *phobic anxiety* dimension (Table 5): subjects who still had no symptoms had lower mean values than those who already had symptoms; subjects that answered “perhaps” were those with the highest mean values. Carriers that answered “no” ( $n = 30$ ) or “perhaps” ( $n = 9$ ) presented significant differences for *somatization* [ $F(3, 189) = 3.966, p = .016; \eta^2 = .218$ ].

Subjects that considered having severe [ $M (n = 11) = 11.33$ ] and moderate [ $M (n = 7) = 10.86$ ] symptoms had higher means in *somatization* than those subjects that present minimal symptoms

Table 2

BSI total, nine dimensions and three indexes (*M*, *SD* and  $\alpha$ ) at the cutoff points of 4, 7 and 10 years

	4 years ( <i>n</i> = 65)		7 years ( <i>n</i> = 95)		10 years ( <i>n</i> = 42)	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
	$\alpha$		$\alpha$		$\alpha$	
BSI Total	36.28	33.72	36.65	28.24	31.32	24.41
	(.97)		(.97)		(.96)	
Somatization	4.15	5.28	4.39	4.67	3.01	3.51
	(.88)		(.87)		(.80)	
Obsessive-compulsive	5.42	4.71	5.85	4.49	5.13	3.79
	(.86)		(.87)		(.77)	
Interpersonal sensitivity	2.72	2.82	2.97	2.61	2.55	2.45
	(.80)		(.79)		(.78)	
Depression	4.58	4.97	4.53	4.49	3.25	3.00
	(.88)		(.89)		(.77)	
Anxiety	3.75	4.19	3.96	3.37	3.61	3.27
	(.84)		(.78)		(.84)	
Hostility	3.97	3.85	4.15	3.47	3.30	2.70
	(.85)		(.86)		(.75)	
Phobic anxiety	1.68	3.31	1.62	2.55	2.00	2.75
	(.85)		(.77)		(.67)	
Paranoid ideation	4.49	4.38	4.54	3.76	4.40	3.41
	(.84)		(.83)		(.76)	
Psychoticism	2.72	3.42	2.51	3.21	1.90	2.48
	(.75)		(.82)		(.77)	
GSI	0.68	0.64	0.69	0.53	0.59	0.46
PSTI	21.02	14.19	23.00	14.87	20.10	12.43
PSDI	1.55	0.53	1.42	0.44	1.41	0.37

Note: BSI = Brief Symptom Inventory; GSI = Global Severity Index; PSTI = Positive Symptoms Total Index; PSDI = Positive Symptom Distress Index; *M* = Mean; *SD* = Standard deviation;  $\alpha$  = Cronbach's alpha

*Table 3*  
Comparison of means for the gender variable: BSI total, four dimensions and two indexes (*M, F, df, p and η<sup>2</sup>*)

	<i>n</i>	<i>M (SD)</i>	<i>F</i>	<i>df</i>	<i>p</i>	<i>η<sup>2</sup></i>
BSI Total	Female (118)	39.48 (33.01)	5.007	1, 193	.026	.026
	Male (85)	29.87 (22.37)				
Somatization	Female (118)	4.81 (5.24)	7.397	1, 193	.007	.037
	Male (85)	2.99 (3.48)				
Interpersonal sensitivity	Female (118)	3.13 (2.77)	4.480	1, 193	.036	.023
	Male (85)	2.33 (2.36)				
Depression	Female (118)	4.91 (4.70)	5.701	1, 193	.018	.029
	Male (85)	3.40 (3.80)				
Phobic anxiety	Female (118)	2.17 (3.31)	6.596	1, 193	.011	.033
	Male (85)	1.11 (1.89)				
GSI	Female (118)	0.75 (0.62)	5.007	1, 193	.026	.026
	Male (85)	0.56 (0.42)				
PSTI	Female (118)	23.55 (14.70)	4.070	1, 193	.045	.020
	Male (85)	19.51 (13.19)				

Note: BSI = Brief Symptom Inventory; GSI = Global Severity Index; PSTI = Positive Symptoms Total Index; *M* = Mean; *F* = Snedecor's F Distribution; *df* = degrees of freedom; *p* = *p*-value; *η<sup>2</sup>* = effect size

*Table 4*  
Comparison of means for marital status variable: BSI total, six dimensions and one index (*M, F, df, p and η<sup>2</sup>*)

	<i>n</i>	<i>M (SD)</i>	<i>F</i>	<i>df</i>	<i>p</i>	<i>η<sup>2</sup></i>
BSI Total	Single (104)	29.36 (25.44)	3.899	3	.010	.060
	Married (89)	36.85 (28.71)				
	Divorced (5)	62.22 (50.43)				
	Widow (2)	15.67 (2.89)				
Somatization	Single (104)	2.60 (3.55)	4.169	3	.007	.066
	Married (89)	4.51 (4.54)				
	Divorced (5)	7.33 (9.30)				
	Widow (2)	1.00 (1.73)				
Obsessive-compulsive	Single (104)	4.66 (3.14)	4.235	3	.006	.064
	Married (89)	5.60 (4.46)				
	Divorced (5)	10.22 (7.98)				
	Widow (2)	5.67 (0.58)				
Depression	Single (104)	4.11 (4.41)	4.121	3	.007	.062
	Married (89)	4.09 (4.13)				
	Divorced (5)	9.11 (6.72)				
	Widow (2)	2.00 (0.00)				
Anxiety	Single (104)	3.38 (3.17)	2.762	3	.043	.043
	Married (89)	3.90 (3.55)				
	Divorced (5)	6.78 (6.57)				
	Widow (2)	1.33 (0.58)				
Phobic anxiety	Single (104)	0.68 (1.17)	4.789	3	.003	.073
	Married (89)	2.10 (3.12)				
	Divorced (5)	3.56 (4.53)				
	Widow (2)	0.33 (0.58)				
Paranoid ideation	Single (104)	3.49 (3.21)	3.820	3	.011	.058
	Married (89)	4.80 (3.92)				
	Divorced (5)	7.33 (5.92)				
	Widow (2)	1.33 (1.15)				
GSI	Single (104)	0.55 (0.48)	3.899	3	.010	.060
	Married (89)	0.69 (0.54)				
	Divorced (5)	1.17 (0.95)				
	Widow (2)	0.29 (0.54)				

Note: BSI = Brief Symptom Inventory; GSI = Global Severity Index; *M* = Mean; *F* = Snedecor's F Distribution; *df* = degrees of freedom; *p* = *p*-value; *η<sup>2</sup>* = effect size

Table 5  
Comparison of means for the variable "Still without symptoms?": BSI total, eight dimensions and three indexes ( $M$ ,  $F$ ,  $df$ ,  $p$  and  $\eta^2$ )

	$n$	$M$ ( $SD$ )	$F$	$df$	$p$	$\eta^2$
BSI Total	Yes (67)	29.62 (25.76)	8.042	2	.001	.142
	Perhaps (9)	67.22 (35.09)				
	No (30)	44.92 (33.97)				
Somatization	Yes (67)	3.06 (4.22)	13.925	2	.000	.218
	Perhaps (9)	10.44 (6.60)				
	No (30)	7.00 (5.20)				
Obsessive-compulsive	Yes (67)	4.88 (4.20)	5.264	2	.007	.095
	Perhaps (9)	9.89 (5.03)				
	No (30)	6.48 (5.24)				
Interpersonal sensitivity	Yes (67)	2.43 (2.26)	5.823	2	.004	.104
	Perhaps (9)	5.44 (2.65)				
	No (30)	3.19 (3.10)				
Depression	Yes (67)	3.40 (3.75)	5.377	2	.006	.097
	Perhaps (9)	7.56 (4.59)				
	No (30)	5.44 (4.88)				
Anxiety	Yes (67)	3.24 (3.30)	4.682	2	.011	.086
	Perhaps (9)	6.33 (3.81)				
	No (30)	5.11 (4.14)				
Hostility	Yes (67)	3.51 (3.56)	4.888	2	.009	.089
	Perhaps (9)	7.56 (5.66)				
	No (30)	5.07 (4.28)				
Paranoid ideation	Yes (67)	3.66 (3.35)	3.675	2	.029	.068
	Perhaps (9)	6.56 (5.68)				
	No (30)	5.48 (4.40)				
Psychoticism	Yes (67)	1.75 (2.45)	5.293	2	.007	.097
	Perhaps (9)	4.89 (4.57)				
	No (30)	3.31 (4.13)				
GSI	Yes (67)	0.56 (0.49)	8.042	2	.001	.142
	Perhaps (9)	1.27 (0.66)				
	No (30)	0.85 (0.64)				
PSTI	Yes (67)	19.61 (12.81)	6.002	2	.003	.104
	Perhaps (9)	35.89 (10.09)				
	No (30)	23.90 (15.99)				
PSDI	Yes (67)	1.41 (0.45)	4.453	2	.014	.085
	Perhaps (9)	1.81 (0.65)				
	No (30)	1.67 (0.51)				

Note: BSI = Brief Symptom Inventory; GSI = Global Severity Index; PSTI = Positive Symptoms Total Index; PSDI = Positive Symptom Distress Index;  $M$  = Mean;  $F$  = Snedecor's F Distribution;  $df$  = degrees of freedom;  $p$  =  $p$ -value;  $\eta^2$  = effect size

[ $M$  ( $n = 16$ ) = 5.73] and those who didn't specified their symptoms in the questionnaire ( $n = 5$ ).

"Has there been a significant change in your life (marriage, divorce, death of loved one, illness, job change, earth, etc.) in recent years?" variable. Significant differences were found concerning somatization, depression, anxiety and hostility dimensions and GSI and PSTI, emphasizing that carriers who experienced meaningful life changes presented higher mean values than those that did not (Table 6).

#### Discussion

This study does not corroborate previous studies suggesting the absence of negative psychological impact resulting from the PST long-term outcome (Timman et al., 2004), because the BSI dimensions values obtained in this sample were higher than

those obtained in previous studies about short-term psychological impact (Lêdo et al., 2013b) and when compared with the standard values reached for the Portuguese population. Nevertheless, and regarding the GSI, PSTI and PSDI, the obtained values did not reflect the presence of clinically psychological disturbance since the PSDI was always inferior to 1.7 (Canavarró, 2007). The lower GSI, PSTI and PSDI scores may be justified by the existence of a self-selection prior to PST of those subjects who were psychologically more prepared (Codori et al., 1994; Paneque et al., 2007; Rolim et al., 2006; Tibben, 2007) and that could be the same who responded to the present study. Subjects who were less psychologically disturbed prior to the PST were those who did not drop out of the follow-ups or did not avoid the reality of the disease (Timman et al., 2004).

Age variable and the *obsessive-compulsive* dimension presented a positive correlation. This may be explained due to

Table 6

Comparison of means for the variable "Has there been a significant change in your life in recent years?": BSI total, four dimensions and two indexes (*M*, *F*, *df*, *p* and  $\eta^2$ )

	<i>n</i>	<i>M</i> ( <i>SD</i> )	<i>F</i>	<i>df</i>	<i>p</i>	$\eta^2$
BSI Total	No (54)	29.27 (27.43)	7.631	1	.007	.070
	Yes (56)	45.77 (33.09)				
Somatization	No (54)	3.58 (4.39)	5.666	1	.019	.051
	Yes (56)	5.94 (5.76)				
Depression	No (54)	3.34 (3.97)	6.991	1	.009	.062
	Yes (56)	5.61 (4.87)				
Anxiety	No (54)	3.00 (3.25)	9.798	1	.002	.086
	Yes (56)	5.21 (3.98)				
Hostility	No (54)	3.49 (3.68)	4.528	1	.036	.041
	Yes (56)	5.15 (4.34)				
GSI	No (54)	0.55 (0.52)	7.631	1	.007	.070
	Yes (56)	0.86 (0.62)				
PSTI	No (54)	19.41 (13.13)	5.334	1	.023	.047
	Yes (56)	25.66 (15.15)				

Note: BSI = Brief Symptom Inventory; GSI = Global Severity Index; PSTI = Positive Symptoms Total Index; *M* = Mean; *F* = Snedecor's F Distribution; *df* = degrees of freedom; *p* = *p*-value;  $\eta^2$  = effect size

a progressive concern with the outbreak of the first symptoms, as suggested by Licklederer, Wolff and Barth (2008). Divorced subjects were those who presented the highest values in almost all BSI dimensions and widows the lowest: that points to the importance of the real/imaginary experiences of rejection/abandonment as realities that might be interfering with these results, instead of the real experiences of loss or feelings of loneliness that might be present with the widowhood (Lêdo et al., 2013b).

Subjects who underwent PST for MJD presented the highest values in *psychoticism* and *phobic anxiety* maybe because MJD patients have shown some emotional changes related to disruption of frontal-subcortical systems (Zawacki, Grace, Friedman, & Sudarsky, 2002) and cognitive disorders (Rezende et al., 2015); although the MJD sample dimension is very small and a previous study conducted with subjects at-risk for MJD showed no psychological disturbance at post-test and after they knew their carriers/non-carriers status (Gonzalez et al., 2004). Additionally, FAP group is aware of a therapeutic solution that prevents progression of the disease to an advanced state (Coelho, Maia, Martins da Silva, Waddington, Planté-Bordeneuve, Lozeron et al., 2012).

All carriers had the highest values in *somatization* and *PSDI*, what is understandable since the carrier condition leads them to be more focused on their physical and body sensations, suggesting that higher levels of *somatization* are associated with real symptoms. The presence of real symptoms appeared to increase the tendency for these individuals to report somatic reactions (Lêdo, Leite, Souto, Dinis, & Sequeiros, 2016; Licklederer et al., 2008), although the perspective that they may probably already have symptoms let them more disturbed than the certainty of having symptoms (Licklederer et al., 2008).

Subjects who had significant changes in their lives were those who presented higher values in *somatization*, *anxiety* and *hostility* dimensions. Being one of the mentioned changes reported the "loss or illness of a close relative" item, it explains the high values on the referred dimensions (Lêdo et al., 2016).

Although the results did not present differences between the psychological impact in the mid- to long-term, they suggest that this impact exists but without being possible to differentiate it regarding the time resulting from the completion and notification of the PST result. So, the age of symptoms onset was not recognized as being determinant to the level of psychological disturbance (Lêdo et al., 2016; Licklederer et al., 2008).

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