Depression levels in Pre-symptomatic Testing for Neurodegenerative Diseases: a psychological point of view

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***Abstract*- The psychological impact of pre-symptomatic testing for some late-onset diseases is still an important topic of study, particularly in the Portuguese population, since there are not many studies published in this field. In a retrospective study, we have investigated the psychological impact, concerning depression indicators, of pre-symptomatic testing (PST) for 3 autosomal dominant late-onset diseases: Huntington disease (HD), Machado-Joseph disease (MJD) and familial amyloidotic polyneuropathy (FAP) ATTRV30M. The study included 686 subjects: 586 (85.4%) were at-risk for FAP ATTRV30M, 92 (13.4%) for HD and 8 (1.2%) for MJD. Among all, 352 received a mutation-carrier result, and 305 a non-carrier result. The majority were women (58.6%). Mean age was 36.3 years (SD, 11,8). Most (50.9%) were single, while 44.5% were married or living with a partner.**

The Beck Depression Inventory (BDI) was completed before testing and againthree weeks, six months and one year after results. Depression scores decreased significantly during the post-testing period, although carriers showed higher values than non-carriers.

Keywords- Depression; BDI; subscales; FAP ATTRV30M; Huntington disease; Machado-Joseph disease; Number of references : 39

I. INTRODUCTION

There are numerous diagnostic and pre-symptomatic tests (PST) for hereditary diseases [1,2,3]. In late-onset neurological disorders (LOND), as Huntington disease (HD), Machado-Joseph disease (MJD) and familial amyloidotic polyneuropathy (FAP) ATTRV30M, the PST will predict accurately if a person will develop symptoms at some time in the future [2,4,5]. The Centre for Predictive and Preventive Genetics (CGPP), at IBMC, provides a counselling protocol for PST of LONDs,with a multidisciplinary team (clinical geneticists and genetic counsellor, clinical psychologists, neurologists, psychiatrist, nurse and social worker).

Thiscounselling protocol for PST in neurodegenerative diseases is a national reference model for genetic counsellingand psychosocial evaluation and support, for persons at risk forthese severe, progressive and debilitating diseases, that have currently no proven effective treatment or cure [2,6].HD, MJD and FAP ATTRV30M are three examples of autosomal dominant neurodegenerative diseases. Each may manifest with a broad spectrum of symptoms [6].

HD is the most studied [5,7,8,9], and its predictive test began to be offered by linkage analysis in 1986, in Canada and the USA [1,10], with direct mutation detection during the 1990's[7-9]. MJD and FAP ATTRV30M have a particularly high prevalence in Portugal. MJD is a cerebellar ataxia, with associated progressive external ophthalmoplegia, extrapyramidal, pyramidal and peripheral signs [11-13]. The V30M mutation in TTR FAP leads to a systemic deposition production of amyloid [14], with a sensorimotor and autonomic peripheral neuropathy [15,16].

FAP ATTRV30M has a slightly earlier onset (mostly 25-35 years, in the classical form), MJD and HD have onset of the first symptoms at a mean around 40 years of age [6]. While FAP ATTRV30M and MJD have mainly neurological symptoms, in HD behavioural problems and cognitive decline are also part of the clinical picture. On the other hand, liver transplantation [17]and, now, some new drug treatments [18] recently came to offer some hope for the families affected with FAP ATTRV30M; MJD and HD still have no treatment, though several clinical trials are still ongoing.

Some psychosocial studies have been done, atCGPP, in these patients and their relatives at-risk [6,19,20,21]. Lêdo [17] studied FAP ATTRV30M carriers,one year after knowing their genetic status, and concluded that there had been no significant emotional distress or feelings of hopelessness. Other studies with subjects at risk for FAP ATTRV30M, HD and MJD pointed to the existence of a psychological well-being and a better health perception than in control subjects [5,6,20].

Also, psychosocial genetic studies were based on the genetic counselling experience of more than 10 years,in individuals at risk [6,24,25]. There has been research published on the importance of contact time with the disease and the parental figures in the psychological impact of PST [21].

In spite of many studies, there are still issuesto be elucidatedregarding the impactof undergoingPST tothese adulthood onset diseases. Studies relating the psychological impactwith the nature of the disease, test resultsand othervariables,such as culturalandsocio-demographic profile continue to be needed. The objectives of this research were to investigate (1) the depression indices before PST and three weeks, six months and one year after receiving the results; and (2) differences in this impact impact related with the type of the disease, a carrier or non-carrier status, and various demographic variables.

II. MATERIALS AND METHODS

A. Type of study

This was a retrospective study, compilingdata from medical records of all subjects at-risk who underwent PST for MJD, HD and FAP ATTRV30M, at CGPP, between 2000 and 2010. All had beenfully counselled and informed about the purpose of this research, during their PST protocol procedure, and consented in writingto the use of their data for this research.

Subjects came for PST on their physiciansadvice after a proband was known in the family, or because other relatives had already been tested at CGPP. Inclusion criteria were (1) to be at a 50% risk (after an affected or carrier parent had been molecularly confirmed), or at 25% risk (if the potentially transmitting parent was deceased); and (2) not showing relevant neurological symptoms.

B. Subjects

Of the 686 subjects of the initial sample, 40 dropped outafter registration and the PST without underwent the psychological evaluation; out of the remaining646, 586 (about 85.4%) were at risk forFAP ATTRV30M, 92 (13.4%) for HD and 8 (1.2%) for MJD. Of the total, 58.6% were women. Mean age was 36.3 years (SD, 11.8); 50.9% were single and 44.5% were living with a partner. Of these 646 subjects, 25 did not receive results, 352 received a mutation carrier result and 305 patients had a mutation negative result.

There were no significant differences in distribution of men and women in relation to age (X^2_{15}= 636-939; p=0.362), marital status (X^2_2= 5.733; p=0.057) or test result (X^2_2= 2.446; p=0.294).

In Table 1, we can see that the number of subjects, which decreased over time. The retention rate at 3 weeks post-testing was 44.0%, at six months post-testing was 19.7%, and at one year post-testing was 9.9%.

TABLE 1.STUDY SAMPLE ALONG THE 4 TIMES STUDIED

Time	n	Gender		Age (yrs)	Marital status	Disease	Testresult
T0	646	Female: *(58,5%)* Male: *(41,5%)*	378 268	Mean: 36.2 SD: 11.8 Range: 14-79	Single: 328 *(50,8%)* Married: 288 *(44,6%)* Divorced: 11 *(1,7%)* Widow: 9 *(1,4%)* Unknown: 10 *(1,6%)*	FAP: 557 *(86,2%)* HD: 81 *(12,5%)* MJD: 8 *(1,2%)*	Carrier: 283 *(43,8%)* Non-carrier: 334 *(51,2%)* Unknown: 29 *(4,5%)*
T1	284	Female: *(58,5%)* Male: *(41,5%)*	166 118	Mean: 36.4 SD: 11.9 Range: 14-78	Single: 145 *(51,1%)* In a couple: 127 *(44,7%)* Divorced: 4 *(1,4%)* Widow: 4 *(1,4%)* Unknown: 4 *(1,4%)*	FAP: 243 *(85,6%)* HD: 37 *(13%)* MJD: 4 *(1,4%)*	Carrier: 138 *(48,6%)* Non-carrier: 138 *(48,6%)* Unknown: 8 *(2,8%)*
T2	127	Female: *(55,1%)* Male: *(44,9%)*	70 57	Mean: 36.5 SD: 11.4 Range: 21-72	Single: 62 *(48,8%)* In a couple: 61 *(48,0%)* Divorced: 0 *(0%)* Widow: 2 *(1,6%)* Unknown: 2 *(1,6%)*	FAP: 103 *(81,1%)* HD: 21 *(16,5%)* MJD: 3 *(2,4%)*	Carrier: 75 *(59,1%)* Non-carrier: 49 *(38,6%)* Unknown: 3 *(2,4%)*
T3	64	Female: *(54,7%)* Male: *(45,3%)*	35 29	Mean: 37.1 SD: 11.7 Range: 21-69	Single: 31 *(48,4%)* Ina couple: 29 *(45,3%)* Divorced: 0 *(0%)* Widow: 2 *(3,1%)* Unknown: 2 *(3,1%)*	FAP: 47 *(73,4%)* HD: 16 *(25%)* MJD: 1 *(1,6%)*	Carrier: 36 *(56,3%)* Non-carrier: 25 *(39,1%)* Unknown: 3 *(4,7%)*

At time 0 (T0, pre-test), there are 40 subjects who underwentthe PST but did not respond to BDI; mostly are women (60%), single, with mean age of 36,3 years and with a PST result of carrier.The fact of not underwent the psychological evaluation may be due to socio-cultural reasons (low education, difficulty reading, understand or answer the questions) and issues of personal nature (subjects did not want to respond to the psychological test); perhaps these subjects were not so prepared to accomplish the PST as their first approach caused them any trouble. Among the remaining times, we also found decreased in the number of subjects; nevertheless, there are common characteristics in these samples of the remaining moments: samples have mostly women with a mean age about 36 years (standard deviation about 11 years), subjects are mostly married or single (in equivalents parts) and mainly at risk for FAP ATTRV30M. At time 1, subjects are mostly non carriers, but as time passes by at evaluation protocol, the number of carriers increases and decreases the number of non-carriers, it means, the carriers are those who mostly remain in the protocol.

C. Procedure

In the context of the protocol for genetic counselling and psychosocial assessment, each subject answered the BDI questionnaire at four moments in time: (1) pre-test (T0): initial psychological evaluation, which included knowing their motivations forundergoing PST, exploring the decision-making processes and coping mechanisms, and detection of emotional states that could prevent a healthy adaptation to the test result; and (2) three weeks (T1), (3) six months (T2) and (4) one year (T3) after communication of

the test result. Interviews were conducted by a clinical psychologist, who applied the depression scale and introduced the data in a database. These time intervals were chosen due to previous studies on HD [4,6,10]. Social and demographic variables (gender, age and marital status) and medical history were also collected at the first psychological assessment.

The variable *depression* was assessed by the version of the BDI translated and validated for the Portuguese population [24, 25]. This scale identifies depression issues, such as sadness, pessimism, sense of failure, dissatisfactionand guilt, expectation of punishment, suicidal ideation, tearfulness, irritability, social withdrawal, indecisiveness, body image distortion, insomnia, fatigue, weight loss, somatic preoccupation and loss of libido [24]. It consists of 21 groups (with four or five statements each, from which the subject has to choose one) intended to cover all the symptoms of depression. The maximum score is 63 (severe depression), and the minimum is zero; a final value equal to or greater than 10 may be indicative of depression; a final value of four or less may signify a possible denial of the subject of his depressive state.

D. Data Analysis

The statistical analysis was performed using the SPSS software package v.19.0 [26]. We used descriptive statistics (frequency, mean, standard deviation, range); bivariate statistics(ANOVA, Pearson correlation coefficients); prediction of numerical results (multiple linear regression, stepwise method) and prediction for the identification of groups (factor analysis and discriminant analysis).

III. RESULTS

A. Analysis of the general frequency of BDI item used for the 4 evaluation stages

We analysed the 21 descriptive items of the scale for the total sample, from T0 to T3(Table 2). At the first evaluation (T0,pre-test) women felt significantly sadder than men and externalized more this emotion through crying. Men showed more punishment feelings than women.

At T1, three weeks after knowing the outcome of the PST, women were sadder than men, but also showed more pessimism and feelings of guilt (Table 3). At T3 and T4, six and 12months after results disclosure, womenstillpresented a higher percentage of symptomatic responsesforalmost all items, althoughthe differencewas notstatistically significant.

B. Exploratory Factor Analysis

The number offactors extractedfor thefactorial analysis of theprincipal componentsbyvarimaxrotation was chosenfromCampos &Gonçalves [27]. Theeigenvaluesof the twofactors(factor 1, cognitive-affective;and factor2, somatic), at the pre-test phase, were respectively5.93and 1.54;at T1thesewere 6.10and 1.68; 5.62and 2.18at T2; and8.36and 1.99at T3, respectively.

InTable 4, we seethat correlation between these two factors,pre-test, was 0.54 (item 12was not considered, since it has not saturated to threshold of 0.35).The correlation between these two factors, at T1, was 0.53 (items 2, 7 and 18 were not considered, since they saturated at both factors atvery similar values).

TABLE 4. FACTORIAL ANALYSIS OF PRINCIPAL COMPONENTS BY VARIMAX ROTATION METHOD TO THE TOTAL SAMPLE AT T0, T1, T2 AND T3

	T0 (pre-test)		T1 (3 wks. after)		T2 (6 mo. after)		T3 (1 yr. after)	
Item	Factor 1 *Cognitive-affective*	Factor 2 *Somatic*	Factor 1 *Cognitive-affective*	Factor 2 *Somatic*	Factor 1 *Cognitive-affective*	Factor 2 *Somatic*	Factor 1 *Cognitive-affective*	Factor 2 *Somatic*
1- Sadness	**.52**	.26	**.46**	.31	**.56**	.19	**.91**	.05
2- Pessimism	**.61**	.27	.48	.45	**.58**	.32	**.67**	-.06
3- Failure	**.62**	.19	**.75**	.12	**.50**	.35	**.55**	.04
4- Displeasure	**.60**	.33	**.56**	.43	**.64**	-.02	**.88**	.02
5- Blame	**.61**	.16	**.71**	.22	.50	.42	**.60**	-.06
6- Punishment	**.49**	.03	**.39**	.12	**.71**	-.01	-.08	**.73**
7- Disappointmentwithhim self	**.65**	.02	.35	.29	.28	-.01	**.65**	-.02
8- Self-criticism	**.61**	.03	**.64**	.07	**.75**	.10	-.07	.10
9- Suicidalideation	**.52**	.23	**.65**	.03	.25	.02	**.77**	-.04
10- Crying	**.48**	.28	**.44**	.23	.09	.17	**.69**	.06
11- Irritability	**.52**	.29	**.48**	.25	**.58**	.28	**.66**	.28
12- Lossofinterest	.29	-.02	**.47**	-.05	**.48**	.34	-.04	**.73**
13- Indecision	**.56**	.27	**.52**	.35	**.52**	.11	**.58**	-.05
14- Appearance	**.52**	.24	.15	**.47**	**.68**	.15	**.79**	.08
15- Lossofenergy	.26	**.63**	.11	**.76**	-.15	**.68**	**.61**	.27
16- Changesofsleeppatterns	.30	**.48**	.23	**.60**	.23	**.72**	.43	.45
17- Fatigue	.32	**.58**	.21	**.73**	.12	**.62**	**.67**	.14
18- Changesappetite	.06	**.63**	.35	.43	.27	**.66**	.26	**.68**
19- Changeweight	-.20	**.61**	-.05	**.49**	.10	**.55**	.53	.46
20- Healthconcerns	.19	**.43**	.09	**.55**	-.12	**.65**	**.70**	.20
21- Lossof sexual interest	.14	**.51**	.23	**.54**	.25	**.49**	**.87**	-.02

The correlation between these two factors, at T2,was 0.45 (item 4 was not considered because of saturating two factors with similar values; in addition, items 6, 8 and 9 were not included because they did not attain the minimum of 0.35 in any of the factors). Correlation between these two factors, at T2, was 0.17 (items 16 and 19 were not considered,asthey saturatedat similar values; in addition, item 8 was not contemplated, because it didnot reach the minimum value of 0.35, in any of the factors).

C. Descriptive analysis for the four moments of assessment

We proceeded to the mean and standard deviation analysis of the results obtained from the BDI scores in four relevant times, for total sample and for women and men samples.

InTable 5, we can see that, the pre-test moment showed the highest values (global:mean=6.73, SD=7.24; men: mean=6.20, SD=6.99; women: mean=7.10, SD=7.40).Women hadalways higher overall averages than men,over the four times, although not statistically significant (T1: p=0.117; T2: p=0.174; T3: p=0.202; T4: p=0.914).

TABLE 5. RESULTS OF THE BDIFOR THE VARIOUS TIME POINTS FOR THE TOTAL SAMPLE, WOMEN AND MEN

	Total		**Women**		**Men**	
	M	*SD*	*M*	*SD*	*M*	*SD*
T0 (pre-test)	6.73 *(n=646; α=0.86)*	7.24	7.10 *(n =378; α =0.86)*	7.40	6.20 *(n =268; α =0.86)*	6.99
T1 (3 wks)	5.11 *(n =284; α =0.87)*	6.23	5.53 *(n =166; α = 0.89)*	6.98	4.51 *(n =118; α =0.81)*	4.97
T2 (6 mo.)	4.47 *(n = 127; α = 0,85)*	5.57	5.04 *(n =70; α 0.86)*	6.26	3.78 *(n =57; α =0.82)*	4.53
T3 (1 yr.)	4.23 *(n =64; α =0.91)*	6.41	4.31 *(n =35; α =0,91)*	6.50	4.14 *(n =29; α =0.91)*	6.42

As the SD was high, we check the number of subjects who had scores higher than the cut-offof 10, at the four points in time: at T0, this number was of 159 (23.18%; mean=17.39, SD=6.54); at T1, we found 47 depressed subjects (6.85%; mean=16.47, SD=6.52); at T2there were 17 (2,48%; mean=16.47, SD=4.94); finally, at T3,the number of depressed subjects was 5 (0.73%; mean=12,40, SD=10,92).

D. Comparison of the total means along the four evaluation moments

We used the*t* test forpairedvariables, in order to solve the problem of*missingcases* observed from T1 to T4.We notedthatthe total averagehad decreasedfromT0 to T3,as we can see in Table 6.

TABLE 6. COMPARISON OF THE VALUES OBTAINED FROM THE APPLICATION OF BDIAT T0, T1, T2 AND T3

Comparison	***mean***	***n***	***T***	***d.f.***	(two-tailed)
T1 T2	7.28 5.11	267 267	5,62	266	0.000*
T 1 T 3	7.34 4.48	120 120	5,45	119	.000*
T1 T4	7.77 4.26	61 61	3,49	60	.001*
T2 T3	4.87 4.42	109 109	1,00	108	.318
T2 T4	5.28 4.60	47 47	,77	46	.446
T3 T4	3.98 4.02	42 42	-,060	41	.956

* P<0.05

We found statistically significantdifferences in thetotaldepression scoresbetween T0 and T1, between T0 and T2,and between T0 and T3.

E. Comparison of the mean for subscales, with socio-demographic variables

Clinically,the meanBDI subscalesrevealed the absence of depressive disorder, sincethe mean values werebelow thecut-off point10 (Table7).We proceeded tocompare these meansregarding the socio-demographic variables, using the *ANOVA* test.

TABLE 7.MEAN OF BDI SUBSCALES ALONG THE FOUR EVALUATION MOMENTS

Time	**Subscales**	**n**	**mean**	**SD**
T0	Cognitive-affective	663	4.18	5.46
	Somatic	663	2.10	2.49
T1	Cognitive-affective	289	2.92	3.86
	Somatic	286	1.62	2.38
T2	Cognitive-affective Somatic	141	2.39	3.61
		140	1.66	2.30
T3	Cognitive-affective Somatic	64	3.25	5.72
		67	0.57	0.96

Over thefour evaluation periods, there were no significant values related to *gender* in any of thesubscales, although, overall, women feltmore depressedthan men; the exception was thesomaticsubscale, at T2 and T1.The*marital status* did not show any significant values.Nevertheless, divorcedsubjects tend to havehigher average valuesthan others.Regarding*age groups*(Table 8)we obtainedsignificant differences at T0(F=5.853,df=5; p=0.000) and T1(F=5.270,df=5; p=0.000), in the somatic subscale: meandepressionwas higher in oldersubjects. At T3, there a wassignificantincreaseof mean values ofdepressionwith advancing age,regarding thecognitive-affective subscale(F=2.627,df=4; p=0.043).

TABLE 8.COMPARISON BETWEEN THE MEAN VALUES OF BDI SUBSCALES WITH AGE GROUPS AT THE FOUR TIMES

Times	Subscales		mean	n	F	P
T0	Cognitive-affective	*17-30*	4.41	259	0.904	0.478
		31-40	3,61	228		
		41-50	4,62	69		
		51-60	4,83	54		
		61-70	4,16	32		
		71-80	3,00	8		
	Somatic	*17-30*	1,89	258	5.853	0.000
		31-40	1,70	229		
		41-50	2,73	70		
		51-60	2,80	54		
		61-70	3,55	31		
		71-80	3,00	8		
T1	Cognitive-affective	*17-30*	2,83	110	1.655	0.546
		31-40	2,59	99		
		41-50	3,39	28		
		51-60	2,28	25		
		61-70	5,00	15		
		71-80	5,50	4		
	Somatic	*17-30*	1,41	109	5.270	0.000
		31-40	1,23	98		
		41-50	1,71	28		
		51-60	2,04	25		
		61-70	4,21	14		
		71-80	4,00	4		
T2	Cognitive-affective	*17-30*	2,69	49	1.107	0.360
		31-40	1,48	48		
		41-50	2,95	19		
		51-60	3,07	14		
		61-70	3,57	7		
		71-80	5,00	1		
	Somatic	*17-30*	1,63	48	1.088	0.370
		31-40	1,17	48		
		41-50	1,74	19		
		51-60	2,07	14		
		61-70	3,00	7		
		71-80	3,00	1		
T3	Cognitive-affective	*17-30*	1,76	21	2.627	0.043
		31-40	2,38	24		
		41-50	3,80	10		
		51-60	8,75	4		
		61-70	8,20	5		
		71-80	0,00	0		
	Somatic	*17-30*	0,52	21	0.523	0.719
		31-40	0,74	27		
		41-50	0,30	10		
		51-60	0,25	4		
		61-70	0,60	5		
		71-80	0,00	0		

In the pre-test evaluation, subjects at risk forFAPand for HD(Table 9), hadsignificantly highermean values in the cognitive-affectivesubscale thanthose subjectsat riskforMJD, although this difference was not significant; nevertheless,three weeksafter the announcementof thePST result(T1), subjects at risk forMJDshowedhigher values,in the samesubscale,though the number of these were very small.Six monthsafter PST result (T2), subjects at risk forMJD andHDhad significantlyhigher values in the cognitive-affective subscalethan thosefromFAPfamilies (F=4.392,df=2;p=0.014), thesame occurringat 12 months(F=3.910,df=2;p=0.025).

TABLE 9. COMPARISON BETWEEN THE MEAN VALUES OF BDI SUBSCALES WITH THE TYPE OF DISEASE OVER THE FOUR TIMES

	Subscales		mean	N	F	
T0	Cognitive-affective	*FAP*	4.14	571	0.886	0.413
		MJD	2,13	8		
		HD	4,64	84		
	Somatic	*FAP*	2,02	570	1.897	0.151
		MJD	2,38	8		
		HD	2,58	85		
T1	Cognitive-affective	*FAP*	2,91	247	0.158	0.854
		MJD	4,00	4		
		HD	2,89	38		
	Somatic	*FAP*	1,52	244	1.564	0.211
		MJD	2,75	4		
		HD	2,13	38		
T2	Cognitive-affective	*FAP*	1,95	112	4.392	**0.014**
		MJD	4,75	4		
		HD	4,00	25		
	Somatic	*FAP*	1,47	111	2.042	0.134
		MJD	2,00	4		
		HD	2,48	25		
T3	Cognitive-affective	*FAP*	2,11	47	3.910	**0.025**
		MJD	8,00	1		
		HD	6,31	16		
	Somatic	*FAP*	0,57	49	0.239	0.788
		MJD	1,00	2		
		HD	0,50	16		

Regarding the*testresult* (Table 10), althoughthere werenosignificant differences, at T2 and T3, consultands found to be mutation carriers had higher meanvaluesin thecognitive-affective subscale.

TABLE10. COMPARISON BETWEEN THE MEAN VALUES OF BDI SUBSCALES WITH THE TEST RESULT FOR FAP

Times	*Subscales*		*mean*	*n*	*F*	*P*
T1	Cognitive-affective	*Non-carrier*	2,90	124	0.005	0.944
		Carrier	2,93	116		
	Somatic	*Non-carrier*	1,70	123	1,177	0,279
		Carrier	1,37	114		
T2	Cognitive-affective	*Non-carrier*	2,76	46	4,965	0,028
		Carrier	1,34	62		
	Somatic	*Non-carrier*	1,76	45	0,987	0,323
		Carrier	1,31	62		
T3	Cognitive-affective	*Non-carrier*	2,73	22	1,064	0,308
		Carrier	1,46	24		
	Somatic	*Non-carrier*	0,50	22	0,243	0,624
		Carrier	0,65	26		

The number of carriers and non-carriers,for each disease Six monthsafter thePSTresult, non-carriersfor FAPhad higher scores than carriers,regarding the cognitiveaffective subscale(F=4.965, df=1; p=0.028); this trend continuedone yearafter results.RegardingHD, although there we nosignificant results, we also foundhigher scoresfornon-carriers. As to MJD, there were only mutation carriers remaining in the study at T1, T2 and T3, and their number was too small.

F. Predictors of the Beck Depression Inventory (BDI)

We aimed to investigate thepredictive value ofvariables that couldexplain thevalues foundin BDI over the evaluation period for the threediseases.Therefore, we opted for amultiple linearregression analysis using a stepwise estimation method [26], thetotal scores of the BDI, as well as ofitscognitive-affective and somatic subscales.We consideredthesocio-demographic dataasindependent variables. We could see thatthe type of disease isthe variablethathas thehighestpredictive valuein the regression equation,explaining4% of the variance of the BDI score, six months after PST result (T2).The *type of disease* and*test result* (R^2=0.10, F=6.316, df=2;p=0.002)explained, overall, 8.1% of variation of thescore at T2(Table 11).

TABLE 11. MULTIPLE LINEAR REGRESSION ANALYSIS

For variables predicting total BDI values at T2						
Model	**Variable**	**B**	**SE**	**β**	**R^2**	***P***
1	Type of disease	2.659	1.071	0.222*	0.04	<0.05
2	Typeofdisease	3,164	1,068	0.264**	.08	<,01
	Testresult	-2,586	1,039	-0.222*		<,05
For variables predicting TotalBDI values at T3						
Model	**Variable**	**B**	**SE**	**β**	**R^2**	***P***
1	Typeofdisease	4,33	1,60	,328**	.09	<,01
For variables predicting Total BDI values at T0						
Model	**Variable**	**B**	**SE**	**β**	**R^2**	***P***
1	Age	0,04	0,01	0,17**	.03	<,01
2	Age	0,04	0,01	0,17**	.04	<,01
	Gender	-0,39	0,20	-0,08*		<,05
For variables predicting the BDI somatic subscale at T1						
Model	**Variable**	**B**	**SE**	**β**	**R^2**	***P***
1	Gender	0,05	0,01	0,24**	.06	<,01
For variables predicting the BDI cognitive-affective subscale at T2						
Model	**Variable**	**B**	**SE**	**β**	**R^2**	***P***
1	Typeofdisease	1,79	0,72	0,24*	.06	<,05
2	Typeofdisease	2,13	0,63	0,29*	.09	<,05
	Testresult	-1,57	0,61	0,22**		<,01
For variables predicting the BDI cognitive-affective subscale at T3						
Model	**Variable**	**B**	**SE**	**β**	**R^2**	***P***
1	Typeofdisease	3,95	1,42	0,34**	.11	<,01

*p<0.05,**p<0.01

It was also foundthat the*type of disease*had apredictive power in theregression equation,explaining 32.8% of the variance of the BDI score at T3, one year after the test result (R^2=0.11, F=7.345, df=1;p=0.009). The *age* and *gender*had apredictive power (R^2=0.04, F=12.027, df=1;p=0.000), explaining 3.3% of the variance of the depression score, at T0 (pre-test). The *type of disease* and *test result*hadpredictive power (R^2=0.10, F=7.591, df=2;p=0.001), explaining 9.0% of the variance in theBDI cognitive-affective subscale, at T2(Table 13).Lastly, the *type of disease*also presented apredictive value (R^2=0.11, F=7.746, df=1; p=0.007), explaining 11.3% of the variance of the BDI cognitive-affective subscale, one year after test results (T3).

IV. DISCUSSION

The number of patients leaving the protocol over one year was veryhigh. This can, of course, bias the conclusions we draw from the data obtained. On the other hand, carriers remain in the protocol more often than non-carriers; therefore, it is necessary to take into account as one of the limitations of this study.

From thedescriptive analysis, as previous studies suggested [3,29], we found thatwomen showedhigher values ofdepression; this seems to corroborate studies that show that depression is more common among women [30].

In thepre-testphase, themean valueswere higher, decreasing along time, a tendencyobservedfor both genders.Similarly to other investigations [3,5,6,19,29,31],the mean valueswerealways below thecut-off(scoreof 10) that would indicatea depressivedisorder, suggestingthe absence ofa negative psychological impactresulting fromthe decision to take PST or its outcome. Also, as suggested before,this maybe justifiedby aprior self-selection of those subjects who are morepsychologically prepared [3,5,6,31],or the existence ofapersonality structurethat hasbetterdefencemechanisms, or that repressesall thatmaybe disturbing tothem,thus avoidthinking about areality thatcausespsychic pain [19]. Thislast pointis relevantif we consider that,in the original versionof theBDI, the authors point tocases wherea total score less than four may indicate a possibledenialof thesubject regarding his depressed state. Another limitation of this work was the absence of data about the subjects who were taking antidepressant or anxiolytic drugs.

We obtainedacceptable resultsof internal consistency inthe BDI scale,since theαvaluesfrom T0 to T4, andfor all groupsof subjects, were greater than0.80, meaning thiswas an instrumentvalid for thisstudy population. It hashighinternal consistency, such as those foundin standardization studies forPortuguese population [25] or other [37].

It is clearthat women, in the pre-test phase, appearsadderthan men, though menhadmore feelingsof punishment; thewomen'sexperienceof the PST includedmore exteriorization of emotions. Inthe first assessment after result disclosure(T1), women continued toshowsadness(and pessimism) as the most evident feeling, while in menthat was guilt, which seems toenhancethe experienceof punishmentthatfollowedthe first step of PST.

The data may suggest that the higher values of depressive symptoms before PST may mean that the decision to undergo genetic testing is a trigger of emotions. Thiswould corroboratethe need forpsychological support from the beginningof the genetic counsellingprocessforPST,as suggested by Weil [32] and Sequeiros [33]. However, we lack a comparison with those who did not undergo PST. On the other hand, this also reinforces the ideathat the genetic counselling protocol andPST offer an advantage, byreducing uncertainty and the gainof a sense ofcontrol regardingthedisease [6,21,34], to those who decide to come for testing and complete it, regardless of the test results.

At allevaluation periods, the cognitive-affective and somaticessentiallytook into account thevaluesfound. This is very similar tonon-clinicalsamples collectedfrom otherstudies [27,35,36],or in clinical samples such as subjects with chronic pain, where authors identified a cognitive and a somatic dimension of depression [37]. Assumingthese asthe twosubscalesof BDI, , we comparedtheirmeanswith socio-demographic and other variables.

There was atendency fordivorcedsubjectsto showthe highest meanin bothsubscales. Though the number of divorced (or widow) subjects was very small,this may imply thatpeoplewho live aloneare more likely to have depressive symptoms,derived from self-perceptionofabsence ofemotional support and more effectivefuture care.

Oldersubjectstended to have higher values in thesomaticsubscale, both pre-test and three weeksafter results; thismayindicate that cognitive or emotional signs of depression are often replaced by somatic symptoms inolder testees. Previous studiesindicateagreater tendencytosomatizationin older consultands [16], suggesting thatdepression,in those cases,is more exteriorized viathe *soma*than the*psyche*. Another possible explanation is that theimpact of the teston them is higher once they arecloser to theage of onsetof their family's disease.

Subjects who underwent PSTforFAP ATTRV30M, consistently showedlower mean scores that in the other two diseases, and significant three weeks after test results. This may be related with a higher hope for treatment in FAPor that liver transplant may halt progression of the disease. Subjects at risk forHD andMJD showedhigher scoresin thecognitive-affective subscale, what may relate to themore threatening clinical symptoms of HD and/or the current absence of cureor treatmentin these diseases [3,38].

Subjects who receivedamutation negative resultfor FAP,had higher valuesin thecognitive-affective subscale sixmonths after knowingtheir genetic status, comparedtothose who prove to be mutation carriers. This mightbe related to theirexperiencewith this diseaseand strong cohesiveness in these families [39]: subjects live, from an early age, with the family's disease, which becomes part of their identity and feelings of belonging. A non-carrier result maylead toaloss ofidentityandfeelingsof survivor guilt.

Though the numbers are very different for each of the three, the *type of disease* is the one with higher predictive value forBDI results. This might again be related to the severity of each disease and their current perspectives for treatment.

Age,gender and, sometimes, the type of diseaseand test resulthave a higher predictivecharacter for depressive indicesamongthe testees. These variables, as well as theirlevelsof psychological functioning, have been widely studied and discussed inthe populationthat undertakes PST [3,5,6,9,34,38]. This is one of themost relevant resultsof our study, for itsclinical relevanceand the need to establish amore timelyinterventionin thoseindividuals identified asvulnerable. Nevertheless, the need for acarefuland personalizedmonitoringto eachindividual whoundergoes PST for such late-onset, incurable and incapacitating diseases,is asubstantialpractical and ethical principlethat still stands [3,11].

V. CONCLUSION

Subjects have higher meandepression levels prior to PST than after disclosure, regardlessof the genetic test result. This stresses the need for a rigorous protocol of genetic counselling and psychosocial evaluation and support, with emphasis on the symbolic representation of the disease and self-coping mechanisms. Another need is perhaps the implementation of therapeutic groups for psychosocial support, so that these subjects can express (or learn to express) their feelings, fears, doubts, etc., decreasing their levels of somatization.

Fromaclinical point of view,there were no values observedthat translatedin a pathological depression; however, we cannotconclude thatPSTfor these diseases do not affect subjects,as defence mechanisms such asdenial andavoidancemay notbring subjects torespond realistically to thedepression inventory items. This is a matter to elaborate on future studies that can evaluate these mental mechanisms, andlead us to a better understanding why people seem not to be so psychologically disturbed when a *bad news*result is disclosed.

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ABLE 2. RESULTS OF BDI FOR THE TOTAL SAMPLE, WOMEN AND MEN

	T0 (pre-test)									**T1 (3 wks after test results)**								
	Total			***Women***			***Men***			***Total***			***Women***			***Men***		
Item	*mean*	*SD*	*%*	*mean*	*SD*	*%*	*mean*	*SD*	*%*	*mean*	*SD*	*%*	*mean*	*SD*	*%*	*mean*	*SD*	*%*
Sadness	**.44**	.10	21	**.54****	1.10	22	.31	.81	17	.29	.81	15	**.54***	1.10	17	.31	.81	13
Pessimism	.52	1.03	27	.55	1.05	28	.47	.99	25	.34	.82	20	**.55****	1.06	24	.47	.99	14
Failure	.34	.77	20	.34	.78	20	.33	.76	20	.24	.66	45	.34	.78	16	.33	.76	12
Displeasure	.30	.71	18	.33	.73	20	.25	.68	15	.31	.75	19	.33	.74	20	.25	.68	19
Blame	.23	.67	14	.20	.60	13	.28	.76	16	.16	.59	8	.20	.60	12	**.28***	.76	5
Punishment	.19	.53	14	.15	.45	12	**.26***	.63	17	.09	.32	8	.15	.45	8	.26	.63	8
Self-disappointment	.13	.41	11	.12	.37	11	.15	.45	12	.09	.31	9	.12	.37	9	.15	.45	8
Self-criticism	.53	.81	39	.54	.84	39	.52	.76	39	.39	.65	33	.54	.84	33	.52	.76	34
Suicidal ideation	.18	.49	14	.18	.49	15	.17	.50	13	.08	.34	7	.18	.49	8	.17	.50	4
Crying	.39	.75	27	.45	**.73***	35	.31	.77	18	.24	.59	19	.45	.74	23	.31	.77	13
Irritability	.50	.75	38	.52	.75	40	.48	.77	36	.46	.75	35	.52	.75	27	.48	.77	34
Loss of interest	.50	60	46	.52	.59	48	.48	.60	44	.48	.53	47	.52	.59	48	.48	.60	45
Indecision	.29	.60	22	.30	.60	23	.29	.62	22	.16	.42	14	.30	.60	16	.29	.62	13
Appearance	.18	.52	13	.15	.46	11	.22	.58	16	.09	.37	8	.15	.46	6	.22	.58	9
Loss of energy	.27	.63	20	.28	.64	20	.26	.63	19	.23	.55	19	.28	.64	19	.26	.63	16
Changes in sleep	.45	.74	32	.49	.74	36	.38	.73	26	.32	.65	23	.49	.74	24	.38	.73	22
Fatigue	.32	.54	29	.33	.55	30	.29	.53	26	.28	.54	24	.33	. 55	26	.29	.53	23
Changes appetite	.24	.53	21	.28	.56	23	.20	.47	17	.24	.50	21	.28	.56	20	.20	.47	22
Change weight	.23	.65	14	.24	.64	15	.22	.67	12	.22	.57	15	.24	.64	16	.22	.67	28
Health concerns	.38	.61	33	.13	.61	32	.39	.61	35	.27	.51	24	.38	.61	23	.39	.61	26
Loss of sexual interest	.21	.58	14	.25	.64	16	.16	.49	12	.19	.56	13	.25	64	15	.16	.49	10

*p <0.05 , **p <0.01

TABLE 3. RESULTS OF BDI AT T3 AND T4 FOR THE TOTAL SAMPLE, WOMEN AND MEN

	T3 (6 monthsafter)									T4 (1 yearafter))								
	Total			**Women**			**Men**			**Total**			**Women**			**Men**		
Item	*M*	*SD*	*%*	*M*	*SD*	*%*	*M*	*SD*	*%*	*M*	*SD*	*%*	*M*	*SD*	*%*	*M*	*SD*	*%*
1- Sadness	.21	.70	11	.29	.82	13	.31	.81	7	.30	.82	15	.37	.94	16	.21	.62	14
2 – Pessimism	.36	.83	21	.37	.85	21	.47	.99	21	.23	.70	13	.27	.77	14	.17	.60	10
3 - Failure	.26	.70	15	.30	.78	16	.33	.76	13	.18	.52	13	.18	.56	13	.17	.47	14
4 - Displeasure	.17	.52	13	.14	.38	12	.25	.68	13	.27	.71	17	.29	.80	16	.24	.58	17
5 – Blame	.10	.48	6	.16	.62	9	.28	.76	2	.07	.26	8	.08	.27	8	.07	.26	7
6 - Punishment	.09	.31	8	.07	.26	7	.26	.63	10	.06	.30	5	.03	.16	3	.10	.41	7
7 - Disappointmentwithhimself	.06	.27	6	.09	.32	7	.15	.45	3	.07	.27	8	.08	.27	8	.07	.26	7
8 - Self-criticism	.24	.50	20	.27	.50	25	.52	.76	15	.13	.34	13	.18	.39	18	.07	.26	7
9 - Suicidalideation	.05	.22	5	.07	.26	7	.17	.50	2	.13	.42	11	.13	.41	11	.14	.44	10
10 - Crying	.25	.65	18	.28	.66	21	.31	.77	13	.19	.45	16	.21	.41	21	.17	.54	10
11 - Irritability	.44	.65	37	.47	.67	40	.48	.77	33	.36	.51	34	.34	.48	34	.38	.56	34
12 - Lossofinterest	.39	.60	35	.44	.59	41	.48	.60	28	.34	.51	33	.37	.49	37	.31	.54	28
13 - Indecision	.16	.41	15	.21	.47	19	.29	.62	10	.13	.39	12	.11	.39	8	.17	.38	17
14 - Appearance	.11	.34	11	.09	.32	7	.22	58	15	.15	.44	12	.16	.50	11	.14	.35	14
15 - Lossofenergy	.28	.57	23	.29	.58	23	.26	.63	23	.30	.70	19	.29	.69	18	.31	.71	21
16 - Changesofsleeppatterns	.28	.61	21	.31	.65	23	.38	.73	20	.19	.50	15	.24	.59	16	.14	.35	14
17 - Fatigue	.30	.48	30	.31	.49	30	.29	.53	30	.30	.58	25	.29	.52	26	.31	.66	24
18 - Changesappetite	.24	.59	17	.25	.61	18	.20	.47	17	.16	.51	11	.16	.50	11	.17	54	10
19 - Changeweight	.17	.51	12	.13	.43	10	.22	.67	15	.13	.34	13	.11	.31	11	.17	.38	17
20 - Healthconcerns	.26	.46	26	.26	.47	25	.39	.61	27	.34	.52	30	.29	.52	26	.41	.68	34
21 - Lossof sexual interest	.18	.53	13	.21	.54	16	.16	.49	10	.28	.67	19	.33	.72	22	.21	.62	14