Genetics and Molecular Biology, 37, 1 (suppl), 263-270 (2014)

www.sbg.org.br

Research Article

Genetic counseling and presymptomatic testing programs for Machado-Joseph Disease: lessons from Brazil and Portugal

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Abstract

Machado-Joseph disease (MJD) is an autosomal dominant, late-onset neurological disorder and the most common form of spinocerebellar ataxia (SCA) worldwide. Diagnostic genetic testing is available to detect the disease-causing mutation by direct sizing of the CAG repeat tract in the ataxin 3 gene. Presymptomatic testing (PST) can be used to identify persons at risk of developing the disease. Genetic counseling provides patients with information about the disease, genetic risks, PST, and the decision-making process. In this study, we present the protocol used in PST for MJD and the relevant observations from two centers: Brazil (Porto Alegre) and Portugal (Porto). We provide a case report that illustrates the significant ethical and psychological issues related to PST in late-onset neurological disorders. In both centers, counseling and PST are performed by a multidisciplinary team, and genetic testing is conducted at the same institutions. From 1999 to 2012, 343 individuals sought PST in Porto Alegre; 263 (77%) of these individuals were from families with MJD. In Porto, 1,530 individuals sought PST between 1996 and 2013, but only 66 (4%) individuals were from families with MJD. In Brazil, approximately 50% of the people seeking PST eventually took the test and received their results, whereas 77% took the test in Portugal. In this case report, we highlight several issues that might be raised by the consultand and how the team can extract significant information. Literature about PST testing for MJD and other SCAs is scarce, and we hope this report will encourage similar studies and enable the implementation of PST protocols in other populations, mainly in Latin America.

Keywords: SCA3, Machado-Joseph, presymptomatic test, ataxia, genetic testing, psychosocial, psychological issues.

Introduction

Machado-Joseph disease (MJD) (MIM #109150), also known as spinocerebellar ataxia type 3 (SCA3), is an autosomal dominant neurodegenerative disease with very high penetrance. MJD/SCA3 is caused by a CAG repeat expansion within the coding region of the ataxin 3 gene, which is located on 14q32 (Kawaguchi *et al.*, 1994). MJD/SCA3 is the most common form of spinocerebellar ataxia (SCA) worldwide (Sequeiros *et al.*, 2012). MJD is more prevalent in populations with Portuguese Azorean ancestry (Gaspar *et al.*, 2001; Castilhos *et al.*, 2013). The extended polyglutamine tract in the mutant protein induces neuronal intranuclear inclusions (NII) and neurodegeneration (Costa and Paulson, 2012). Symptoms generally appear later in life (mean age of 32-40 years) and mainly affect postural balance and the coordination of gait, speech and fine movements of the hands; patients are often confined to wheelchairs and, later, become bedridden (Sequeiros and Coutinho, 1993; Jardim *et al.*, 2001). Currently, there is no effective treatment to delay or halt the progression of this disease (Costa and Paulson, 2012); how-

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ever, some manifestations can be alleviated by treatment with specific drugs and using a multi-professional supportive approach including speech and physiotherapy.

Diagnostic genetic testing is available to detect this mutation by directly measuring the length of the CAG repeat (Maciel *et al.*, 2001). Genetic counseling provides patients with information about the familial form of the disease and the presymptomatic test (PST) and facilitates the decision-making process, which can sometimes be difficult depending on the nature of the information provided by the consultand about the patient's genetic status (Guimarães *et al.*, 2013). PST identifies the individuals who are at risk of developing the disease if they live long enough. PST for late-onset neurological diseases became available in 1983 for Huntington's Disease (HD) (European Community Huntington Disease Collaborative Study Group, 1993), and the counseling procedure developed for HD was used as a model in subsequent programs (Wiggins *et al.*, 1992; Broadstock *et al.*, 2000). Specific guidelines have emerged from discussions between experts and non-professional organizations and have enabled the development and maintenance of PST programs with good acceptance, resolution, and ethical quality (International Huntington Association (IHA) and the World Federation of Neurology (WFN) Research Group on Huntington's Chorea, 1994); these guidelines were recently revised and updated (MacLeod *et al.*, 2013).

There is limited literature on the PST for SCAs (Sequeiros, 1996a). MJD does not affect cognitive capacities (Rolim *et al.*, 2006a), which might increase the uptake of PST for MJD relative to HD. State of the art PST for MJD among Portuguese-speaking populations might help elucidate the peculiarities of this disorder and the cultural differences among the affected families. Two such PST protocols were implemented in Portugal (Sequeiros, 1996b) and Porto Alegre, Brazil (Rodrigues *et al.*, 2012). Both protocols encompass other hereditary ataxias, Huntington's disease, familial amyloidotic polyneuropathy (FAP) ATTRV30M, and other neurodegenerative diseases. The main aims of these programs are to provide the at-risk individuals with genetic information on their family's disease through genetic counseling, to disclose the genetic status (mutation carrier or non-carrier) to consenting individuals, to facilitate informed decision-making and effective coping upon receipt of the test results, and to provide psychosocial and neurological support. In this paper, which is dedicated to Latin American human and medical geneticists and students, we present our experience gained from two programs conducting PST for MJD in Porto and Porto Alegre, and report an illustrative counseling case.

Methods

PST protocols for MJD in Rio Grande do Sul, Brazil and Porto, Portugal

The Brazilian protocol

The present PST program was initiated at the Hospital de Clínicas de Porto Alegre (HCPA), Porto Alegre, Brazil, in 1999 (Rodrigues *et al.*, 2012). Porto Alegre is the capital of the of state of Rio Grande do Sul (10 million inhabitants), and HCPA is the reference center for the PST program. Consultands must be adults at risk for a late-onset neurological disease that was diagnosed in a close relative and perceive themselves as asymptomatic; consultands might also be individuals with minor signs of disease, when they are in doubt (or denial) about their clinical status. Until 2009, the program team included a medical geneticist, a neurologist, and a clinical psychologist. After a survey on the acceptance of PST at HCPA (Rodrigues *et al.*, 2012), improvements were made to the program (Table 1). Since 2010, the team has expanded to include a genetic counselor and a psychiatrist. A specific clinic for PST was installed at the genetics outpatient facility.

The structure of the counseling sessions is also summarized in Table 1. The first session involved the core staff. After discussing themes related to diagnosis, prognosis, risk, and others, the protocol was explained, reaffirming that the consultand was free to opt out at any time without any loss of confidentially or other rights. A comprehensive psychodynamic approach was favored, in which the consultands' motivation to take the test was explored, and the consultands were stimulated to envisage their behavior in face of the possible test results and the potential psychological, familial and social consequences of the results. The psychiatrist also evaluated aspects of the consultand's mental status, such as attention, affect, humor, critical judgment, content, course of thought, and personality traits. The second and third sessions were conducted by the psychologist or psychiatrist. In the fourth session, the core staff and the consultand reviewed the motivations and issues raised during the psychological sessions, and a final follow-up of genetic information was provided. If the consultand decided to take the test, a blood sample was collected. The core staff conducted the disclosure session, which occurred up to three months later. The consultands were accompanied by another person to this session.

For follow-up, evaluations were offered and scheduled at three weeks, as well as six and 12 months after the disclosure of the results. If the consultand dropped out of the program, no further effort was made to call the individual back, out of respect to his/her decision. All the data were maintained in protected written files. Neurological assessment and further genetic counseling sessions were available upon the patient's request.

Table 1 - Similarities and differences between the Portuguese and Brazilian programs for genetic counseling and presymptomatic testing.

		Porto (Portugal)	Porto Alegre (Brazil)
Team		Clinical geneticist, genetic counselor, psychologist, neurologist, psychiatrist and social worker	Clinical geneticists, genetic counselor, clinical psychologist, neurologist, and psychiatrist
Enrollment criteria		To be at 50% risk, 18 years or older, asymptomatic* (both Programs)	
Pretest	1st visit	- genetic counseling - psychology evaluation - first blood sample taken	- genetic counseling: core staff
	2nd visit	3 weeks after 1st visit: - genetic counseling - social worker's evaluation - consent form signed -second blood sample taken	1 to 2 weeks after 1st visit: - psychological assessment with psychologist or psychiatrist
	3rd visit	3 weeks after 2nd visit: - communication of results	1 to 2 weeks after 2nd visit: - new session with psychologist/psychiatrist
	4th visit	No	1 to 2 weeks after 3rd visit: - 2nd genetic counseling - blood collection
	5th visit	No	- when results are ready: - communication of results
	Neurological evaluation	Always available, but only upon referral of the team (both Programs)	
	Psychiatrist? Social worker?	Upon referral of the team Yes	Yes No
	Number of blood collections	2	1
	Signed consent form	Yes	No
Disclosure of results		3rd visit	5th visit
Post-test follow-ups		3 weeks and 6 and 12 months after disclosure: psychologist or psychiatrist. 12 months after disclosure: neurologist	3 weeks and 6 and 12 months after disclosure: psychologist or psychiatrist
Follow-ups upon request		Clinical geneticist, counselor, and/or social worker	Clinical geneticist, counselor, social worker, and/or neurologist

* For more details and exceptions, see text.

The Portuguese protocol

Portugal has 10 million inhabitants. A National Program for Genetic Counseling and PST for MJD was set up in 1995 (Sequeiros, 1996a,b) and includes centers in major cities and areas with high disease prevalence (Porto, Coimbra, Lisbon and Azores). Here, we describe the experience gained at the Center for Predictive and Preventive Genetics (CGPP) in Porto, where the PST program was first set up.

The PST protocol has been described in detail elsewhere (Sequeiros, 1996b) and is shown in Table 1. The clinic was devoted to PST because the affected patients were followed at their local hospitals. The multidisciplinary team is composed of clinical geneticists, a genetic counselor, clinical psychologists, neurologists, psychiatrist, and a social worker. The consultand was advised to bring a support person, who should not be a sibling or other at risk relative, to all visits. Consultands must be at least 18 years old and at 50% risk. Consultands at 25% risk may be accepted if the potential transmitting parent was unavailable. Individuals aged 16 years or older may also be tested if reproductive decisions, including prenatal diagnosis, need to be made. The first session was conducted by a clinical geneticist or genetic counselor; informative support was offered regarding the symptoms and natural history of MJD, the cause of the disease, its mode of inheritance, genetic risk and burden, variable age of onset and severity, and unavailable treatment and reproductive options. The laboratory procedure was explained; if the consultand consented, the first blood sample was taken, and the DNA was stored until the second appointment. The clinical psychology evaluation consisted of structured anamnesis and psychometric tools to evaluate motivations, explore the decision-making process and coping mechanisms, and detect emotional distress, cognitive or psychiatric problems that might threaten good adjustment to the test results. A referral to the team psychiatrist was made when appropriate. Other explored topics included the anticipated advantages/disadvantages, projected changes after testing, to whom the consultands would disclose the results and intrafamilial communication of risks. Social evaluation explored and reinforced the importance of familial support and social networks and probed potential social changes and new needs after testing. In the second visit, genetic counseling evaluated the comprehension of the information that was previously received, clarified possible doubts and misconceptions, and prepared the consultand for the communication of the results. Only then was the laboratory procedure initiated.

For follow-up, evaluations were recommended at three weeks, six months and one year after disclosure of the

results. Annual neurological follow-up was offered to the mutation carriers.

Laboratory procedure

Molecular analysis was performed once at the HCPA and twice at the CGPP, and the procedure has been described elsewhere (Maciel *et al.*, 2001). Both centers follow the OECD Guidelines for Quality Assurance in Molecular Genetic Testing (2007) and the European Molecular Quality Genetics Network (EMQN) Best Practice Guidelines for Molecular Genetic Testing of the SCAs, spinocerebellar ataxias (Sequeiros *et al.*, 2010), and perform external quality assessment (EQA) for the SCAs (Seneca *et al.*, 2008) using the EMQN.

Results

Summary of the Brazilian experience

Between 1999 and 2009, 184 individuals (18/year) at risk for an autosomal dominant, adult-onset neurological disease sought genetic counseling for PST at the HCPA; 147 (80%) of the individuals were at risk for MJD, and the majority of the remaining patients were at risk for HD. One hundred subjects (51%) decided to provide a blood sample (82 at risk for MJD, 56%); 92% of the individuals who provided a blood sample returned to receive their results. Surprisingly, none of the individuals returned for the post-test evaluations. A full description of this 10-year experience has been previously presented (Rodrigues *et al.*, 2012).

Since 2010, modifications to the protocol led to increased access to the program. Therefore, we will present this group separately. Over a period of three years (January 2010 to December 2012), 159 individuals sought PST counseling (53/year); 116 (73%) of these individuals were at risk for MJD. Fifty percent of all individuals (81/159) decided to take the test and received their results, a number similar to that observed in the 10 previous years. However, unlike the former period, 31% of the tested individuals returned for post-test consultations.

Summary of the Portuguese experience

Since 1998, more than 1,248 persons (from the whole country) at risk for a late-onset neurological disease reported to the CGPP. Of these individuals, 236 (19%) were at risk for MJD, whereas most were from families with HD (39%) or FAP ATTRV30M (31%) families. While genetic testing for MJD and HD began at the CGPP in mid-1998, testing for PAF ATTRV30M only began in 2006.

Between 1996 and 2013, 1,530 individuals (90 per year) at risk for a late-onset neurological disease sought genetic counseling and PST at the outpatient clinic in Porto. Sixty-six (4.3%) individuals were at risk for MJD, and 51 (77%) individuals agreed to the test; of these 51 individuals, 25 (49%) returned for the post-test follow-up.

Between 1999 and 2009 (identical to the period reported for Porto Alegre), 1,159 individuals at risk for a late-onset neurological disease requested PST (105 per year) at the Porto center. Only 24 of them (2%) were at risk for MJD; 17 of these (71%) individuals decided to take the test, and all of them returned to receive their results. However, only 4 (24%) returned for at least one post-test evaluation.

An illustrative case

Here, we present an illustrative case of the process of genetic and psychodynamic counseling during PST for MJD; all names are fictitious. Maria, 38, asked for preliminary information on her son's, Bruno, risk. Bruno is a gifted football player on the verge of being hired by a European club. Maria's husband, Juliano, adopted Bruno during his first year of life. Bruno is aware that Juliano is a foster parent, and they have an excellent relationship. Bruno does not know who his biological father is. He was conceived during an affair between Maria and a famous football player named Pedro, who moved overseas when Maria was pregnant. Maria was deeply resentful of this separation, to the point of failing to disclose the father's identity to her son. She avoided any contact regarding Pedro, even in newspapers or television. However, she supported Bruno's decision to become a football player. Juliano neither appreciated nor encouraged this, perhaps out of jealousy directed towards Pedro.

Two months ago, Maria was visited by Pedro's sister, Fernanda, who told her that Pedro had died under strange circumstances in a car accident. Considering this information and the impending move of her son to Europe to play football, Maria felt pressured to reveal to Bruno the identity of his biological father and tell him of his father's death. However, according to Fernanda, the car crash was suggestive of a disguised suicide. Pedro had a long history of intermittent alcohol abuse and depression, and the "accident" happened soon after Pedro began having problems with coordination. Furthermore, Fernanda revealed that another brother of hers and Pedro's had been diagnosed with Machado-Joseph Disease and that their father committed suicide several years ago after developing gait ataxia. Fernanda explained to Maria the 50% risk of first-degree relatives carrying this mutation, which led her to seek PST in another city, and she advised Maria to tell Bruno about his family history.

Maria was afraid of telling Bruno about his biological father and his potential disease risk. She did not completely understand the risk and was unaware that PST for this disease is not recommended for minors. She believed that once Bruno became aware of the facts, his impulsive temperament would lead him to get tested immediately. She was also concerned about the consequences to Bruno's new work contract if the family history or test results were revealed in the press or social networks.

During the interview, Maria conveyed to the counselors several data suggestive of Fernanda's insights, such as the events leading to Pedro's likely suicide and the disease risk for Bruno. However, Maria did not appear to understand all the issues related to Bruno's genetic risk. She also seemed to ignore the problems caused by a lack of open communication and trust between family members. Although intelligent and emotionally healthy, Maria brought up two contradictory points: she came to obtain information about potential PST for her son, but simultaneously said that she "would not dream of letting Bruno come for testing".

What are the ethical issues related to this case?

Family members have a moral obligation to share genetic information with each other. Wertz *et al.* (2003) stated that "the ethics of disclosure of genetic risks begins with intra-familial duties to warn and protect family members from harm". Fernanda followed this moral obligation by giving her nephew the opportunity to know that he is at risk. He may choose to be tested or not. Maria has not understood all the risks, and she seems confused about her duty to reveal this information to Bruno.

Whenever possible, professionals should promote understanding in children and adolescents about their disorders or their risk for disorders. However, there is a consensus that knowledge of the fact alone does not constitute competence to request or consent to testing (Wertz *et al.*, 2003).

All international guidelines advise against testing children and adolescents in the absence of medical benefit (pre-symptomatic testing). This consensus considers the increasing respect for minors' autonomy in the overall context of medical care (Wertz *et al.*, 2003). The age at which the emotional and legal maturity required for consent are attained is variable; it depends on the social background and the severity of the disease. In the present case, despite being 17 years old, Bruno is starting a career, with rights and duties identical to those of an adult. The decision regarding testing must be assessed on a case-by-case basis and must be anchored by bioethical and psychological advice when needed, as in this case. Bruno is at risk for MJD; he is the son of a suicidal father and a candidate to receive a diagnosis of an incurable disease.

To avoid potential discrimination, genetic testing results should not be disclosed to third parties (employers, insurers, schools, and governmental agencies), particularly for a severe and incurable disease. In careers accompanied by the media, such as football, the harm from possible exposure and publicity regarding a family illness or even PST is multiplied.

What are the psychological issues related to this case?

The principal issue at stake is to provide support to Maria for her to understand her own mental mechanisms, to help her communicate with her son. A psychodynamic view pointed to the coexistence, in Maria's mind, of a clear knowledge *and* a clear refusal of that knowledge. As with other defense mechanisms, this complex and primitive mechanism of splitting with disavowal of the ego is present in both severe mental disorders and in normal people. Our consultand was not aware of her inner contradiction or why this splitting occurred. She is faced with difficult decisions. She must address the potential effects on Bruno's teenage mind when he receives such information (his biological father's identity, having a famous biological father, his and his father's coincidental choice of profession, the nature of his father's death, his risk of being a carrier of an unknown genetic disease, and its potential effects on his career). With a splitting/disavowal defense, an individual can `know' *and* `not know'. There are dual consequences of this defense mechanism in Maria's mind. Maria knows several important facts about Bruno. By not informing him, she thinks she is doing him good and not causing harm. If Maria does not understand what is happening in her mind, her mind could remain split, and she would not be able to communicate the truth to her son, leading to more harm and suffering.

Aided by counselors, Maria should manage to arrive at a good solution: telling her son the truth, accepting some resentment against her, and working to eventually repair the affected family bonds.

How should the staff handle this case?

Counselors should clarify the risks to Maria and help her understand her difficulties in telling her 17-year-old son his father's identity. Maria is the only link between the counselors and the person at risk. A psychodynamic insight here is very important because it might allow Maria to alleviate her guilt towards Bruno and Juliano, so that she can finally talk to her son about his father and his own genetic risk.

The genetic counseling and PST team members also face risks, pressures and challenges, including how to maintain personal and professional integrity and therefore, comply with any of the decisions that Bruno might take in the future, as well as how to comply with the time Maria will need to communicate the truth to her son. It would not be surprising if the same mental mechanism of splitting/disavowal appeared in a staff member or in the team as a whole: knowing this is a difficult decision-making process and simultaneously urging instant communication without the proper preparation. Even a prepared professional could identify with either the mother or the son and could fear the potential psychological, social and economic losses to this talented player. Both situations would be

harmful. If the health-care professional identifies with the consultand, he/she could drive the mother to continue hiding the family history, identity and death of her son's father, as well as his genetic risks. Therefore, it is important that the PST staff remain alert to countertransference reactions. To avoid these countertransference risks, it is recommended that the team include a psychiatrist or other professional trained in psychodynamics.

Discussion

This report highlights the differences between requesting and accepting test results in PST programs in Brazilian and Portuguese populations. These data suggest that reviewing and reformulating the PST programs might increase their accessibility. This study offers motivation and stimulus to individuals interested in the field of human genetics. Using a case report, we highlight the various issues that can be raised by a consultand and illustrate how the PST team must be able to detect the layers of significant information.

The decision to undergo PST for late-onset neurological diseases is mainly a question of awareness and accessibility. These factors have most likely led to the greater number of PST requests in Portugal relative to Brazil during the same time period despite similar population sizes (10 million); 1,159 requests were made in Portugal, whereas only 184 were made in Porto Alegre. Brazil is a large and rapidly developing country with 200 million inhabitants, but the country only has one established PST program. One reason for this is the lack of medical genetics facilities and the lack of recognition of genetic testing in the Brazilian Public Health System (Melo and Sequeiros, 2012, Horovitz *et al.*, 2012). A simple change in the Porto Alegre PST program, the opening of a specific outpatient clinic staffed by a cohesive multidisciplinary team, led to a 200% increase in requests (from 18 to 54/year) for PST, proving the importance of accessibility.

While 80% of the requests came from MJD families in Porto Alegre, only 4% were from MJD families at the Porto center. This difference is related to the epidemiology of the late-onset neurological conditions. MJD is quite common in southern Brazil, with a minimal prevalence of 4:100,000 inhabitants (Prestes *et al.*, 2007), whereas the overall Portuguese prevalence is 2:100,000, as determined by a systematic population-based survey (Coutinho *et al.*, 2013). However, 2/3 of the consultands in Porto come from FAP ATTRV30M families, which has the largest global prevalence (90.3:100,000) in Póvoa/Vila do Conde (Sousa *et al.*, 1995) in the northwest coast of Portugal.

The differences in the acceptance to undergo testing are more elusive and cannot be inferred from the present data. However, some suggestions can be made. The 50% acceptance to undergo PST for MJD among those who initially sought the test in Porto Alegre remained constant despite the program changes in 2010. In contrast, the acceptance to undergo PST for MJD was 77% at the Porto center. One possible explanation is that the Portuguese individuals who sought PST were better informed about the inheritance and genetic risks of the disease than the Brazilian individuals, and therefore, were more likely to be tested. The self-selection of consultands prior to requesting PST has been previously noted (Codori *et al.*, 1994); those who are not informed, not prepared to know or simply do not want to know do not come for genetic counseling (Bernhardt *et al.*, 2009). If that is the case, there might be several more individuals in Portugal than in Brazil who are at risk for MJD but do not request PST. The numbers of requests for PST in late-onset neurological diseases (115/year in Portugal and 53/year in Porto Alegre, which services the entire state of Rio Grande do Sul and has a similar population to that of Portugal) do not support this. We suggest that the Portuguese population might be more favorable than the southern Brazilian population to PST testing. This is a complex issue related to other degrees of freedom and choice. For instance, in Brazil, pregnancy interruption for genetic disorders is not legal. Some Brazilian consultands argued that because they would not be allowed to ask for a future pregnancy interruption, there was no reason to undergo PST. In addition to this hypothesis, it is important to consider the cultural and social differences between these two populations, including the perceptions of health and disease, and the specific population profiles, such as the avoidance of uncertainty.

Another difference between the two centers is the number of blood samples analyzed for each consultand: 2 samples in Porto and 1 in Porto Alegre. The Porto Alegre laboratory initially tested the consultands twice. No differences were observed between the 1st and 2nd samples. Based on the consistency of results and the economical cost involving the duplicate blood collection and laboratory analysis, it was decided that one sample would be sufficient for testing.

There are fewer studies on PST for MJD and other SCAs than for HD; these studies mainly encompass the Portuguese, Cuban, French and Brazilian experiences (Paúl *et al.*, 1999; Lima *et al.*, 2001; Goizet *et al.*, 2002; Gonzalez *et al.*, 2004; Rolim *et al.*, 2006a,b; Cecchin *et al.*, 2007; Paneque *et al.*, 2007a,b, 2009; Gonzalez *et al.*, 2012; Cruz-Mariño *et al.*, 2013; Guimarães *et al.*, 2013) (Paiva RSR, 2006, PhD thesis, UNICAMP, Campinas). We hope this report will encourage similar studies in other populations, mainly in Latin America.

As in medicine in general, the four main ethical principles that should be followed in genetic counseling and PST programs are beneficence, autonomy, non-maleficence and equity (Wertz *et al.*, 2003). Because no curative or preventive treatment is available for the majority of neurodegenerative diseases, such as HD, MJD and other SCAs, there is no direct medical benefit to performing PST. However, the potential benefits include better psychosocial

well-being and a better control over life decisions and future planning, including reproductive decisions, educational and professional choices, and financial, medical and other arrangements for the future. The principle of autonomy requires that the test should be limited to at risk adults who are mentally capable of making that decision. The initiation of testing should begin with the at risk individual; the health staff should not initiate contact but should encourage patients to inform their families. Before the test is performed, the consultands should be fully informed about the disease and the *a priori* risks of being affected, the inexistence of preventive or curative therapies, and the limitations in predicting the age of onset, severity, and course of the symptoms. The privacy of the patients and relatives and confidentiality of their personal, clinical and genetic data, by avoiding unauthorized access of the results to third-parties including employers, insurers, the education system, adoption agencies, or even family doctors, relatives and friends, are critical for non-maleficence. Among the psychosocial risks of PST are depression, disruption of family life, and social stigmatization. In certain cases, depression and "survivor's guilt" can appear in the individuals whose tests are normal. All of these aspects must be discussed with the consultand. Therefore, supportive pre- and post-test counseling should be offered to all consultands, regardless of their test results (Wertz *et al.*, 2003).

Finally, equity in access (the ethical principle of justice) should be guaranteed (Wertz *et al.*, 2003). This is one of the main challenges that health professionals, in general, and medical geneticists and counselors, in particular, still face in Latin America: to fight for equal opportunities and accessibility to all and for a fair distribution of income and access to health care and information in our populations. If we can improve medical and genetic literacy and stimulate the creation of new PST centers, our journey to a better world has already begun.

Acknowledgments

We would like to thank Joana Teixeira and Victor Mendes (Porto) and Karina Donis (Porto Alegre) for their technical assistance and contribution in data gathering, as well as all of the professionals in both teams who conduct the Porto and the Porto Alegre genetic counseling and PST programs. Additionally, we would like to thank the patients and families who have sought our care. This work was supported by Fundo de Incentivo à Pesquisa do Hospital de Clínicas de Porto Alegre (FIPE-HCPA), Project GPPG HCPA 06-482. CMO and FR were funded by INAGEMP - Instituto Nacional de Genética Médica Populacional. LSF and LBJ are funded by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

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