Multidisciplinary Elements in Approaching Huntington's disease

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Abstract

Huntington's disease stands out as one of the most complicated and complex disorders confronted by human beings. The changes and adaptations which it imposes within the affected patients but also their families makes it stringent for specialists - including mental health professionals - to engage their attention and resources to obtaining an as profound understanding of Huntington's disease as possible.

The present paper is a theoretical review which proposes to bring to attention and to promote the idea of multidisciplinary approach of the disease in order to both support the health professionals in their quests of treating their patients but also to inform the people affected about the fact that efforts are being mobilized by scientists in order to understand and solve Huntington's challenges. We should consider, maybe in a greater measure that its hereditary nature manifests in such manner that it increases not only the stress usually associated to the onset itself but also the fear of being a victim of a high probability of losing one's self to Huntington's disease - fear quite persistent among the patients' offspring. Also, we consider this diagnosis to be worthy of extensive research efforts.

Keywords: *Huntington's disease, chorea, balance disorder, reduced flexibility, stem cells.*

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I. INTRODUCTION

Huntington's disease is a degenerative disorder, incurable at the present moment. The first description of this complicated disease was provided in 1872 by George Huntington (Paulson & Albin, 2011). According to data from literature the life expectancy after the onset of this disease is somewhere around 20 years, and the symptomatology is progressive, chronic (Bates, Tabrizi, & Jones, 2014).

The patients carry a gene called Huntington, which carries an additional segment, with a certain sequence of repeating units. When the segment has an increased size it creates an erroneous protein production (Ross & Tabrizi, 2011), with destructive effect. Currently, information about the appearance and disease progression are limited.

Huntington's disease is caused by a genetic defect on chromosome 4. It is an inherited disease, with autosomal dominant transmission, linked to the mutation of a gene located on the short arm of chromosome 4. This gene encodes the "Huntington" protein (Walker, 2007). This contains a sequence of repetitive units of trinucleotide cytosine-adenine-guanine (CAG) at one of its ends. In healthy subjects, the number of repetitions of the CAG triplet is variable and ranges between 11 and 32 (Ashizawa, Zoghbi, & Appel, 1997). Patients affected by Huntington's disease have 40 or more CAG trinucleotides. The higher the number of repetitions is then the more precocious is the start of the disease.

II. DESCRIPTION OF THE SYMPTOMATOLOGY

There are two types of Huntington's disease. The most common is the adult-onset Huntington's disease which is present in individuals whose symptoms appears at the middle age of 39 or 40 years. A form with early onset of Huntington's disease is present in a small number of cases and begins in childhood or adolescence (Nance, & Myers, 2001).

The clinical psychologist and the psychiatrist can identify symptoms expressed by: antisocial behaviors, hallucinations, irritability, mood disorders, anxiety, paranoia, psychosis, memory loss, speech disorders, confusion or disorientation (Leroi, & Michalon, 1998; Anderson, & Marder, 2001); some authors support the possibility of identifying psychological or psychiatric symptoms that can act as a predictor of Huntington's disease, such as depression, anxiety and

symptoms of obsessive - compulsive disorder; in this population, the mentioned symptoms manifest themselves in a more striking manner, before the onset of disease (Duff et al., 2007).

As for motility, with a progressive manifestation (Walker, 2007), there may appear abnormal movements such as facial movements, uncontrollable movements, rapid and sudden movements of the arms, legs and face and other body parts and also impermanent walking. To establish a diagnosis, the doctor will perform a physical examination and will assess the patient's family history; beside their complaints (patients typically seek medical attention due to the deterioration of work capacity - Walker, 2007). A neurological exam will also be applied. The doctor may see signs of: dementia, abnormal movements, abnormal reflexes, hesitant speech or enunciation difficulty. A tomography can show the loss of cerebral tissue, especially deep inside the brain. The genetic tests represent a special value for diagnosis and prediction (Margolis & Ross, 2003).

III. APPROACHES IN IDENTIFYING THE WAYS OF TREATMENT FOR HUNTINGTON' S DISEASE

Currently, there are no specific treatments for Huntington's disease (Rosenblatt, & Leroi, 2000; Sarkar et al., 2008); it is therefore important to know the treatment options that address different levels of patient functioning. Some symptoms can be treated with medication and different methods of therapy (Ross, & Tabrizi, 2011).

The doctor may prescribe medicines to treat depression (its incidence being double among patients with Huntington compared to the general population - Paulsen et al., 2005), to control involuntary movements and antipsychotic drugs in order to manage mental symptomatology. Depression and suicidal symptomatology are common among people with Huntington's disease (Paulsen et al., 2014), which is why it is important for all those who take care of a person with Huntington's disease to monitor symptoms and treatment. As the disease progresses, patients will require assistance and supervision (Bates, Tabrizi, & Jones, 2014). Lastly it will require 24-hour care.

There is also a series of studies which support that a possible treatment for Huntington's disease could be the use of stem cells (Lindvall & Koka, 2006; Ryu et al., 2004). Researchers have constructed a special type of brain cells that could help restoring muscle coordination deficits. Zhang (2010) and his colleagues have demonstrated that severe motor deficits observed in a mouse

with Huntington's disease could be corrected by implanting cells created in labs. In this study, the group focused on what is known as GABA neurons, cells whose degradation is responsible for the disruption of a key neuronal circuit and the loss of motor functions in patients with Huntington. According to the authors, GABA neurons produce a key neurotransmitter, a chemical substance that underlies the communication network in the brain which helps coordinate movement (Zhang, An, Montoro & Ellerby, 2010).

In the laboratory, Zhang and his colleagues learned how to make large amounts of GABA neurons from human embryonic stem cells, which they have tried on a mouse with Huntington's disease. The purpose of the study was to see if the cells could integrate in safe conditions into the brain of the mouse. To their astonishment, the cells not only did integrate, but they reestablished the destroyed communication network, restoring the right of efficiency of the motor functions (Zhang et al., 2010). This study suggests the possibility of using stem cells as a treatment for Huntington's disease in the future but also the malleability of which the adult brain can be modeled (Lindvall & Kokaia, 2006).

A study conducted by Zinzi, Jacopini, Frontali and colleagues (2007), supports the use of nonpharmaceutical treatments such as rehabilitation and nutrition.

The effects of an intensive multidisciplinary rehabilitation program on a sample of 40 persons have shown that the treatment has positive effects on motor and functional performances of patients suffering from the disease even from the early stages without any psychiatric symptoms. In the early stages, when the minimum deficiencies (chorea, balance disorder, reduced flexibility) and functional limitations (difficulty in activities necessary for daily tasks, at the workplace or at home) are present, balance and basic stability can be useful to prevent falls and to delay the onset of mobility restrictions. Also, respiratory therapy can help maintain the lung capacity and to induce relaxation. The authors also show the potential of exercises to maintain a good cardiovascular system as being important in order to prevent additional limitations or deficiencies. Patients must be encouraged to maintain their regular activity for as long as possible. Occupational therapy is also recommended because it can play a relevant role in this regard, helping patients adjust to new conditions, promoting safety and delaying the loss of social role at work and at home. The study included patients in the early stages among which can be encountered attention and memory deficiencies reduced processing speed, decreased flexibility and decision making capacity (Zinzi et al., 2007). In later stages the functional limitations are severe. Rehabilitation approach should

be dedicated mainly in the prevention of secondary complications, such as muscle contractures, chest infections, but also respiratory infections (Moskowitz, & Marder, 2001; Cook, 2004). From the point of view of nutrition, a hyper caloric diet, especially in the early and middle stages of the disease, is an empiric treatment. The amount of calories to be added must be evaluated based on the weight loss and the real intake from food (Morales et al., 1998; Trejo et al., 2004).

A study (Vaddadi, Soos, Chiu & Dingjan, 2002) showed the fact that unsaturated fatty acids are beneficial towards addressing Huntington's disease. Creatine, a compound produced endogenously and exogenously which is acquired through diet, appears to be a relevant component in maintaining the cellular energy (Andreassen et al., 2001).

There is evidence that suggest that oxidative stress appears in the early stages of the disease, together with mitochondrial dysfunction, both of these things leading to an energy deficiency of the patients. The addition of antioxidants could be beneficial in these circumstances, but at the moment there is no concrete data regarding this.

While the dysphasia progresses and the nutrition produces various problems to the patients, dried food should be avoided in favor of the moist food, cutting it into small pieces or grinding it. It is possible that patients may require help finishing their meal. In many institutions, they currently use feeding tubes. Feeding time represents a moment where patients can receive the attention and affection of the caregivers, can socially interact, and this might help them. Therefore it is preferable that a caregiver helps the patient to swallow and not use feeding tubes (Ranen, Nance, & Paulsen, 1999). Although artificial nutrition can improve the lifespan, some patients refuse to be artificially fed and react negatively when they are proposed such a solution (Hunt & Walker, 1989). Using life support should be discussed with patients in advance, when they are capable of understanding medical explanations, when speech and knowledge are still strong and it is possible to make significant choices.

IV. CONCLUSIONS

Huntington's disease is a long lasting disorder, of neurological nature, which can be transmitted to descendants (Went, Vegter-Van der Vlis & Bruyn, 1984).

These aspects have profound implications for those affected, which means that patients and their families will require extensive care and support, generation after generation.

The ideal caretaking model for patients is to create a multidisciplinary team that includes several health specialists (neurologists, psychiatrists, rehabilitation therapists, psychologists, genetic counselors, nurses, social workers) that also includes family members and the information received from them in order to make a plan on how to approach the patient (McMurray, 2001).

For the patients care there must be used a personalized approach (Ranen, Nance, & Paulsen, 1999). Although symptoms and functional difficulties are the same for all individuals there are other things that must also be taken into account such as individual characteristics and personality of each patient and internal and external factors which may influence them.

The ability to cope with the disease, previous interests, the place where he worked, the people who were close differentiate the way in which the people suffering from this disease should be treated.

Also, the social environment can have a more or less positive influence towards the patient's behavior. Familial environment, the type of work which is mostly intellectual or physical, external sources of aid, interpersonal relationships have a certain importance in treating the disease. Because of the genetic implications of the disease, the medical team should also be oriented towards caring and being supportive towards the entire family (Ross et al., 2014).

We believe that the multidisciplinary team, in the case of disease Huntington's, is not only recommended in building a intervention plan for patients with this diagnosis but also in the conduct of researches that takes into account the possibility of addressing any type of factor that could contribute to transmission, the onset and progress of the disease.

References

Anderson, K. E., & Marder, K. S. (2001). An overview of psychiatric symptoms in Huntington's disease. *Current psychiatry reports, 3*(5), 379-388.

Andreassen, O. A., Dedeoglu, A., Ferrante, R. J., Jenkins, B. G., Ferrante, K. L., Thomas, M., ... & Beal, M. F. (2001). Creatine increases survival and delays motor symptoms in a transgenic animal model of Huntington's disease. *Neurobiology of disease, 8*(3), 479-491.

Ashizawa, T., Zoghbi, H., & Appel, S. (1997). Diseases with trinucleotide repeat expansions. *Current neurology, 17*, 79-135.

Bates, G., Tabrizi, S., & Jones, L. (Eds.). (2014). *Huntington's disease*. Oxford University Press.

Cook, O. Q. B. (2004). Huntington's disease. *Physical Management in Neurological Rehabilitation, 221*.

Duff, K., Paulsen, J. S., Beglinger, L. J., Langbehn, D. R., Stout, J. C., & Predict-HD Investigators of the Huntington Study Group. (2007). Psychiatric symptoms in Huntington's disease before diagnosis: the predict-HD study. *Biological psychiatry, 62*(12), 1341-1346.

Hunt, V. P., & Walker, F. O. (1989). Dysphagia in Huntington's disease. *Journal of Neuroscience Nursing, 21*(2), 92-95.

Leroi, I., & Michalon, M. (1998). Treatment of the psychiatric manifestations of Huntington's disease: a review of the literature. *Can J Psychiatry, 43*(9), 933-940.

Lindvall, O., & Kokaia, Z. (2006). Stem cells for the treatment of neurological disorders. *Nature, 441*(7097), 1094-1096.

Margolis, R. L., & Ross, C. A. (2003). Diagnosis of Huntington disease. *Clinical chemistry, 49*(10), 1726-1732.

McMurray, C. T. (2001). Huntington's disease: new hope for therapeutics. *Trends in neurosciences, 24*(11), S32-S38.

Moskowitz, C. B., & Marder, K. (2001). Palliative care for people with late-stage Huntington's disease. *Neurologic clinics, 19*(4), 849-865.

Morales, L. M., Estevez, J., Suarez, H., Villalobos, R., de Bonilla, L. C., & Bonilla, E. (1989). Nutritional evaluation of Huntington disease patients. *The American journal of clinical nutrition, 50*(1), 145-150.

Nance, M. A., & Myers, R. H. (2001). Juvenile onset Huntington's disease—clinical and research perspectives. *Mental retardation and developmental disabilities research reviews, 7*(3), 153-157.

Paulsen, J. S., Hoth, K. F., Nehl, C., Stierman, L., & Huntington Study Group. (2014). Critical periods of suicide risk in Huntington's disease. *American Journal of Psychiatry*.

Paulsen, J. S., Nehl, C., Hoth, K. F., Kanz, J. E., Benjamin, M., Conybeare, R., ... & Turner, B. (2005). Depression and stages of Huntington's disease. *The Journal of neuropsychiatry and clinical neurosciences, 17*(4), 496-502.

Paulson, H. L., & Albin, R. L. (2011). Huntington's disease: Clinical features and routes to therapy.

Ranen, N. G., Nance, M. A., & Paulsen, J. S. (1999). *A Physician's Guide to the Management of Huntington's Disease*. New York: Huntington's disease Society of America.

Rosenblatt, A., & Leroi, I. (2000). Neuropsychiatry of Huntington's disease and other basal ganglia disorders. *Psychosomatics, 41*(1), 24-30.

Ross, C. A., & Tabrizi, S. J. (2011). Huntington's disease: from molecular pathogenesis to clinical treatment. *The Lancet Neurology, 10*(1), 83-98.

Ross, C. A., Aylward, E. H., Wild, E. J., Langbehn, D. R., Long, J. D., Warner, J. H., ... & Tabrizi, S. J. (2014). Huntington disease: natural history, biomarkers and prospects for therapeutics. *Nature Reviews Neurology*, *10*(4), 204-216.

Ryu, J. K., Kim, J., Cho, S. J., Hatori, K., Nagai, A., Choi, H. B., ... & Kim, S. U. (2004). Proactive transplantation of human neural stem cells prevents degeneration of striatal neurons in a rat model of Huntington disease. *Neurobiology of disease, 16*(1), 68-77.

Sarkar, S., Krishna, G., Imarisio, S., Saiki, S., O'Kane, C. J., & Rubinsztein, D. C. (2008). A rational mechanism for combination treatment of Huntington's disease using lithium and rapamycin. *Human molecular genetics, 17*(2), 170-178.

Trejo, A., Tarrats, R. M., Alonso, M. E., Boll, M. C., Ochoa, A., & Velásquez, L. (2004). Assessment of the nutrition status of patients with Huntington's disease. *Nutrition, 20*(2), 192-196.

Vaddadi, K. S., Soosai, E., Chiu, E., & Dingjan, P. (2002). A randomised, placebo-controlled, double blind study of treatment of Huntington's disease with unsaturated fatty acids. *Neuroreport, 13*(1), 29-33.

Walker, F. O. (2007). Huntington's disease. *The Lancet, 369*(9557), 218-228.

Went, L. N., Vegter-Van der Vlis, M., & Bruyn, G. W. (1984). Parental transmission in Huntington's disease. *The Lancet, 323*(8386), 1100-1102.

Zhang, N., An, M. C., Montoro, D., & Ellerby, L. M. (2010). Characterization of human Huntington's disease cell model from induced pluripotent stem cells. *PLoS currents*, 2.

Zinzi, P., Salmaso, D., De Grandis, R., Graziani, G., Maceroni, S., Bentivoglio, A., Zappata, P., Frontali, M., Jacopini, G. (2007). Effects of an intensive rehabilitation programme on patients with Huntington's disease: A pilot study. *Clin. Rehabil, 21*(7), 603-613.