WHAT IS HUNTINGTON'S DISEASE AND HOW WE CAN USE VIRTUAL REALITY TO OVERCOME DIFFICULTIES?

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Abstract

Huntington's disease, or HD, is a rare, neurodegenerative disease that causes the progressive breakdown (degeneration) of nerve cells in the brain. The molecular cause of HD is a mutation in the HTT gene, which codes for the Huntingtin protein. A part of the gene segment contains the repeating base pairs CAG, as illustrated. Normally, the base pairs CAG repeat 10-35 times, however in an individual with HD the segment repeats 36-120+ times. This produces an abnormally long protein. Fragments get cut off into toxic fragments that bind together and accumulate in neurons, damaging them. This paper specifically looks at the role of miRNAs in the pathogenesis of HD and the development of a novel application designed to provide comprehensive support to HD patients and the history behind HD. This application offers virtual, interactive physical therapy to alleviate physical symptoms while simultaneously monitoring disease progression.

Introduction

Anyone can develop this disease, but it is most common in people of European descent. Because Huntington's disease is an autosomal dominant disease, meaning the mutated gene that causes the disease is on one of the non-sex chromosomes and as little as one copy of the mutated gene from either parent is enough to cause it, it affects both sexes equally and, when someone with HD has a child, the child has a 50 percent chance of inheriting the disease. Symptoms of Huntington's disease, such as amnesia and mental confusion, paranoia, depression, and mood swings, and difficulty moving with slow or rigid movements, usually appear when the patient reaches 30 to 50 years of age.

Huntington's disease currently lacks a cure, but various treatments aim to manage its symptoms and enhance the quality of life for affected individuals. Medications like tetrabenazine help control chorea, while antipsychotic drugs, antidepressants, and mood stabilizers address behavioral and mood-related symptoms. Physical and occupational therapies focus on maintaining mobility and independence, while speech therapy aids in preserving communication skills and addressing swallowing difficulties. Supportive care encompasses psychological support and counseling, while genetic counseling assists with understanding inheritance patterns and making informed family planning decisions. Ongoing research and clinical trials continue to explore new treatments and approaches for Huntington's disease.

Symptoms:	The first symptoms of Huntington's disease often include: ● difficulty concentrating ● memory lapses ● depression – including low mood, a lack of interest in things, and feelings of hopelessness ● stumbling and clumsiness ● mood swings, such as irritability or aggressive behavior Over time, someone with Huntington's disease may develop: ● involuntary jerking or fidgety movements of the limbs and body ● difficulty speaking clearly – eventually they may find all communication very difficult ● swallowing problems – they may choke on food and get lung infections (pneumonia) from food going down the wrong way ● increasingly slow or rigid movements ● personality changes – sometimes they may change so they don't seem like their former self at all ● breathing problems ● difficulty moving around – they may eventually lose the ability to walk or sit up by themselves	Huntington's disease - Symptoms - NHS

Current therapies and/or inventions to	There is no treatment that can stop or reverse HD, but some of the	Huntington's Disease | National Institute of

assist patients:	symptoms can be treated: ● The drugs tetrabenazine and deuterabenazine can treat chorea associated with HD ● Antipsychotic drugs may ease chorea and help to control hallucinations, delusions, and violent outbursts ● Drugs may be prescribed to treat depression and anxiety ● Several groups of scientists are using gene-editing or specific molecules that can interfere with the production of HTT in cells or animals to reduce or eliminate the production of HTT.	Neurological Disorders and Stroke

Breakthrough

Our scientific breakthrough uses miRNA administered through the spinal fluid of the patient. Additionally, we just performed a labster on using microRNA to treat a cancer patient. Similar to the labster, the hope is our scientific breakthrough will use microRNA to interfere with a mutation in the genome of the patient.

The brain still needs Huntingtin protein, healthy huntingtin protein can be grown then inserted into people through spinal fluid.

There has been a lot of research done into the potential of using miRNA in neurodegenerative diseases, one of them being the use of synthetic microRNA for silencing the mutation that causes ALS at UMass in two patients, administered through spinal fluid. It proved the use of miRNA to treat ALS was possible, and is currently being altered for efficacy before more trials. THis, along with the research of other scientists shows the viability of using miRNA to treat HD.

Molecular causes:	Mutations in the HTT gene cause Huntington disease. The HTT gene provides instructions for making a	Huntington disease: MedlinePlus Genetics

	protein called huntingtin. Although the function of this protein is unclear, it appears to play an important role in nerve cells (neurons) in the brain. The HTT mutation that causes Huntington disease involves a DNA segment known as a CAG trinucleotide repeat. This segment is made up of a series of three DNA building blocks (cytosine, adenine, and guanine) that appear multiple times in a row. Normally, the CAG segment is repeated 10 to 35 times within the gene. In people with Huntington disease, the CAG segment is repeated 36 to more than 120 times. People with 36 to 39 CAG repeats may or may not develop the signs and symptoms of Huntington's disease, while people with 40 or more repeats almost always develop the disorder. An increase in the size of the CAG segment leads to the production of an abnormally long version of the huntingtin protein. The elongated protein is cut into smaller, toxic fragments that bind together and accumulate in neurons, disrupting the normal functions of these cells. The dysfunction and eventual death of neurons in certain areas of the brain underlie the signs and symptoms of Huntington's disease.	

How it works

By delivering virtual, interactive physical therapy to patients in order to relieve their physical symptoms while also tracking the trajectory of their sickness, this invention seeks to give patients total support. Patients, their physicians, and researchers alike gain from this as data gathered by the invention can be utilized to evaluate the efficacy of various treatments. The technology takes the shape of many strategically positioned patches that track a patient's

motions and muscle activity. Real-time feedback is then sent to the patient to adjust their actions during virtual physical therapy. In order to achieve this, in addition to the input provided by the patches themselves, the devices will be equipped with sensors such as gyroscopes, accelerometers, and MyoSensors. Additionally, vibration motors will be used, which supply the physical feedback that is typically absent from at-home physical therapy.

The patient will receive information from the app regarding the purpose of the patches and the best area to apply them on their body. Additionally, data will be gathered by the app to display how the illness is developing over time and whether it has gotten better or worse. Since the app is intended for use by physicians, patients, and researchers, the information it gathers will assist physicians in prescribing the best course of action and assist researchers in determining which symptoms are best treated with physical therapy. In general, the program will benefit users who experience balance issues, irregular gait, slow and inflexible movement, and difficulties moving—all indications of Huntington's disease.

Conclusion

The life of an individual with Huntington's disease and their family is significantly affected by this terrible illness. We hope to help patients and physicians suffering with HD using our technology, app, and scientific discovery.

References

Ardekani, A. M., & Naeini, M. M. (2010). The Role of MicroRNAs in Human Diseases. *Avicenna Journal of Medical Biotechnology*, *2*(4), 161–179. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3558168/ Defranco, M. (n.d.). *Physical Therapy in Huntington's Disease*. https://hdsa.org/wp-content/uploads/2015/02/HDSA_PPT-for-Physical-Therapy.pdf *Huntington's Disease: Genetics, Juvenile Cases & Chorea*. (n.d.). Cleveland Clinic. https://my.clevelandclinic.org/health/diseases/14369-huntingtons-disease#:~:text=Who%20does%20Huntington *Huntington disease: MedlinePlus Genetics*. (n.d.). Medlineplus.gov. https://medlineplus.gov/genetics/condition/huntington-disease/#frequency *Huntington's Disease*. (n.d.). National Institute of Neurological Disorders and Stroke. https://www.ninds.nih.gov/health-information/disorders/huntingtons-disease#:~:text=Treating%2 Kazilek. (2016, April 5). *Ignoring Genes*. Askabiologist.asu.edu.

https://askabiologist.asu.edu/ignoring-genes Lee, S.-T., Chu, K., Im, W.-S., Yoon, H.-J., Im, J.-Y., Park, J.-E., Park, K.-H., Jung, K.-H., Lee, S. K., Kim, M., & Roh, J.-K. (2011). Altered microRNA regulation in Huntington's disease models. *Experimental Neurology*, *227*(1), 172–179. https://doi.org/10.1016/j.expneurol.2010.10.012 Mueller, C., Berry, J. D., McKenna-Yasek, D. M., Gernoux, G., Owegi, M. A., Pothier, L. M., Douthwright, C. L., Gelevski, D., Luppino, S. D., Blackwood, M., Wightman, N. S., Oakley, D. H., Frosch, M. P., Flotte, T. R., Cudkowicz, M. E., & Brown, R. H. (2020). SOD1 Suppression with Adeno-Associated Virus and MicroRNA in Familial ALS. *New England Journal of Medicine*, *383*(2), 151–158. https://doi.org/10.1056/nejmoa2005056 *Silencing of an ALS gene safely delivered to patients in UMass Medical School study*. (2020, July 8). UMass Chan Medical School. https://www.umassmed.edu/news/news-archives/2020/07/silencing-of-an-als-gene-safely-delivered-to-patients-in-umass-medical-school-study/ NHS Choices. (2019). *Symptoms - Huntington's disease*. NHS. https://www.nhs.uk/conditions/huntingtons-disease/symptoms/ Quinlan, S., Kenny, A., Medina, M., Engel, T., & Jimenez-Mateos, E. M. (2017, January 1). *Chapter Seven - MicroRNAs in Neurodegenerative Diseases* (L. Galluzzi & I. Vitale, Eds.). ScienceDirect; Academic Press. https://www.sciencedirect.com/science/article/abs/pii/S1937644817300515?via%3Dihub