Multiple system atrophy

Description

Multiple system atrophy is a progressive brain disorder that affects movement and balance and disrupts the function of the autonomic nervous system. The autonomic nervous system controls body functions that are mostly involuntary, such as regulation of blood pressure. The most frequent autonomic symptoms associated with multiple system atrophy are a sudden drop in blood pressure upon standing (orthostatic hypotension), urinary difficulties, and erectile dysfunction in men.

Researchers have described two major types of multiple system atrophy, which are distinguished by their major signs and symptoms at the time of diagnosis. In one type, known as MSA-P, a group of movement abnormalities called parkinsonism are predominant. These abnormalities include unusually slow movement (bradykinesia), muscle rigidity, tremors, and an inability to hold the body upright and balanced (postural instability). The other type of multiple system atrophy, known as MSA-C, is characterized by cerebellar ataxia, which causes problems with coordination and balance. This form of the condition can also include speech difficulties (dysarthria) and problems controlling eye movement.

Multiple system atrophy usually occurs in older adults; on average, signs and symptoms appear around age 55. The condition worsens with time, and affected individuals survive an average of 10 years after the signs and symptoms first appear.

Frequency

Multiple system atrophy has a prevalence of 2 to 5 per 100,000 people.

Causes

Multiple system atrophy is a complex condition that is likely caused by the interaction of multiple genetic, environmental, and lifestyle factors. Some of these factors have been identified, but many remain unknown.

Changes in several genes are being studied as possible risk factors for multiple system atrophy. The genetic risk factors with the most evidence are variants in the *SNCA* and *COQ2* genes. The *SNCA* gene provides instructions for making a protein called alpha-synuclein, which is abundant in normal brain cells but whose function is unknown. Studies suggest that several common variations in the *SNCA* gene are associated with

an increased risk of multiple system atrophy in people of European descent. It is unclear whether these variations also affect disease risk in other populations. The *COQ2* gene provides instructions for making a protein called coenzyme Q2. This enzyme carries out one step in the production of a molecule called coenzyme Q10, which has a critical role in energy production within cells. Variations in the *COQ2* gene have been associated with multiple system atrophy in people of Japanese descent, but this association has not been found in other populations. It is unclear how changes in the *SNCA* or *COQ2* gene increase the risk of developing multiple system atrophy.

Researchers have also examined environmental factors that could contribute to the risk of multiple system atrophy. Initial studies suggested that exposure to solvents, certain types of plastic or metal, and other potential toxins might be associated with the condition. However, these associations have not been confirmed.

In all cases, multiple system atrophy is characterized by clumps of abnormal alpha-synuclein protein that, for unknown reasons, build up in cells in many parts of the brain and spinal cord. Over time, these clumps (which are known as inclusions) damage cells in parts of the nervous system that control movement, balance and coordination, and autonomic functioning. The progressive loss of cells in these regions underlies the major features of multiple system atrophy.

Learn more about the genes associated with Multiple system atrophy

- COQ2
- SNCA

Inheritance

Most cases of multiple system atrophy are sporadic, which means they occur in people with no history of the disorder in their family. Rarely, the condition has been reported to run in families; however, it usually does not have a clear pattern of inheritance.

Other Names for This Condition

- MSA
- OPCA
- Progressive autonomic failure with multiple system atrophy
- SDS
- Shy-Drager syndrome
- Sporadic olivopontocerebellar atrophy

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Multiple system atrophy 1, susceptibility to (https://www.ncbi.nlm.nih.gov/gtr/conditions/C3714927/)

Genetic and Rare Diseases Information Center

- Multiple system atrophy (https://rarediseases.info.nih.gov/diseases/7079/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Multiple system atrophy%22)

Catalog of Genes and Diseases from OMIM

- MULTIPLE SYSTEM ATROPHY 1, SUSCEPTIBILITY TO; MSA1 (https://omim.org/entry/146500)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28Multiple+System+Atrophy%5BMAJR%5D%29+AND+%28multiple+system+atrophy%5BTI%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+360+days%22%5Bdp%5D)

References

- Al-Chalabi A, Durr A, Wood NW, Parkinson MH, Camuzat A, Hulot JS, Morrison KE, Renton A, Sussmuth SD, Landwehrmeyer BG, Ludolph A, Agid Y, Brice A, Leigh PN, Bensimon G; NNIPPS Genetic Study Group. Genetic variants of the alpha-synucleingene SNCA are associated with multiple system atrophy. PLoS One. 2009 Sep22;4(9):e7114. doi: 10.1371/journal.pone.0007114. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19771175) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2743996/)
- Fanciulli A, Wenning GK. Multiple-system atrophy. N Engl J Med. 2015 Jan15;372(3):249-63. doi: 10.1056/NEJMra1311488. No abstract available. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/25587949)
- Federoff M, Schottlaender LV, Houlden H, Singleton A. Multiple system atrophy:the application of genetics in understanding etiology. Clin Auton Res. 2015Feb;25(1):19-36. doi: 10.1007/s10286-014-0267-5. Epub 2015 Feb 17. Citation on PubMed (https:

//pubmed.ncbi.nlm.nih.gov/25687905)

- Gilman S, Wenning GK, Low PA, Brooks DJ, Mathias CJ, Trojanowski JQ, Wood NW,Colosimo C, Durr A, Fowler CJ, Kaufmann H, Klockgether T, Lees A, Poewe W, QuinnN, Revesz T, Robertson D, Sandroni P, Seppi K, Vidailhet M. Second consensusstatement on the diagnosis of multiple system atrophy. Neurology. 2008 Aug26;71(9):670-6. doi: 10.1212/01.wnl.0000324625.00404.15. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18725592) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2676993/)
- Low PA, Reich SG, Jankovic J, Shults CW, Stern MB, Novak P, Tanner CM, GilmanS, Marshall FJ, Wooten F, Racette B, Chelimsky T, Singer W, Sletten DM, SandroniP, Mandrekar J. Natural history of multiple system atrophy in the USA: aprospective cohort study. Lancet Neurol. 2015 Jul;14(7):710-9. doi:10.1016/S1474-4422(15)00058-7. Epub 2015 May 27. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/26025783) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4472464/)
- Multiple-System Atrophy Research Collaboration. Mutations in COQ2 in familialand sporadic multiple-system atrophy. N Engl J Med. 2013 Jul 18;369(3):233-44.doi: 10.1056/NEJMoa1212115. Epub 2013 Jun 12. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/23758206)
- Scholz SW, Houlden H, Schulte C, Sharma M, Li A, Berg D, Melchers A, Paudel R, Gibbs JR, Simon-Sanchez J, Paisan-Ruiz C, Bras J, Ding J, Chen H, Traynor BJ, Arepalli S, Zonozi RR, Revesz T, Holton J, Wood N, Lees A, Oertel W, Wullner U, Goldwurm S, Pellecchia MT, Illig T, Riess O, Fernandez HH, Rodriguez RL, Okun MS,Poewe W, Wenning GK, Hardy JA, Singleton AB, Del Sorbo F, Schneider S, Bhatia KP,Gasser T. SNCA variants are associated with increased risk for multiple systematrophy. Ann Neurol. 2009 May;65(5):610-4. doi: 10.1002/ana.21685. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19475667) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3520128/)
- Stemberger S, Scholz SW, Singleton AB, Wenning GK. Genetic players in multiplesystem atrophy: unfolding the nature of the beast. Neurobiol Aging. 2011Oct;32(10):1924.e5-14. doi: 10.1016/j.neurobiolaging.2011.04.001. Epub 2011 May24. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21601954) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3157605/)

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