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## Useful References on the Diagnosis and Management of Multiple System Atrophy

### **Introduction**

The following list is not exhaustive but is a starting point for understanding more about Multiple System Atrophy (MSA).

### **Natural History**

Wenning GK, Geser F, Krismer F, et al & European Multiple System Atrophy Study Group. The natural history of multiple system atrophy: a prospective European cohort study  
Lancet Neurol 2013; 12: 264-274. <http://www.ncbi.nlm.nih.gov/pubmed/23391524>

Low PA, Reich SG, Jankovic J, et al. Natural history of multiple system atrophy in the USA: a prospective cohort study. Lancet Neurol 2015; 14: 710-719.  
<http://www.ncbi.nlm.nih.gov/pubmed/26025783>

Figuroa JJ, Singer W, Parsaik A, et al. Multiple system atrophy: prognostic indicators of survival.  
Mov Disord 2014; 29:1151-7. <http://www.ncbi.nlm.nih.gov/pubmed/24909319>

Coon EA, Sletten DM, Suarez MD, et al. Clinical features and autonomic testing predict survival in multiple system atrophy. Brain 2015; 138: 3623-31. <http://www.ncbi.nlm.nih.gov/pubmed/26369944>

## MSA Useful references

Calandra-Buonaura G, Guaraldi P, et al. Multiple system atrophy with prolonged survival: is late onset of dysautonomia the clue? *Neurol Sci* 2013; 34: 1875-8.

<http://www.ncbi.nlm.nih.gov/pubmed/23728718>

Petrovic IN, Ling H, Asi Y, et al. Multiple system atrophy-parkinsonism with slow progression and prolonged survival: a diagnostic catch *Mov Disord* 2012; 27: 1186-90.

<http://www.ncbi.nlm.nih.gov/pubmed/22806758>

Wenning GK, Ben Shlomo Y, Magalhaes M, et al. Clinical features and natural history of multiple system atrophy. An analysis of 100 cases. *Brain* 1994; 117: 835-45.

<http://www.ncbi.nlm.nih.gov/pubmed/7922469>

Schrag A, Wenning GK, Quinn N, et al. Survival in multiple system atrophy. *Mov Disord* 2008; 23: 294-6. <http://www.ncbi.nlm.nih.gov/pubmed/18044727>

Seppi K, et al. Progression of parkinsonism in multiple system atrophy. *J Neurol* 2005; 252: 91-96. <http://www.ncbi.nlm.nih.gov/pubmed/15654560>

Testa D, et al. Comparison of natural histories of progressive supra nuclear palsy and multiple system atrophy. *J-Neurol Sci* 2001; 22: 247-251.

<http://www.ncbi.nlm.nih.gov/pubmed/11731878>

Walsh RR, Krismer F, Galpern WR, et al. Recommendations of the Global Multiple System Atrophy Research Roadmap Meeting. *Neurology*. 2018; 90: 74-82 Review.

<https://www.ncbi.nlm.nih.gov/pubmed/29237794>

Foubert-Samier A, Traon AP, Guillet F et al. Disease progression and prognostic factors in multiple system atrophy: A prospective cohort study. *Neurobiol Dis* 2020; Feb 19

<https://www.ncbi.nlm.nih.gov/pubmed/32087288>

Kaufmann H, Norcliffe-Kaufmann L, Palma JA, et al. Autonomic Disorders Consortium. Natural history of pure autonomic failure: A United States prospective cohort. *Ann Neurol* 2017; 81: 287-297. <https://www.ncbi.nlm.nih.gov/pubmed/28093795>

## **Diagnosis**

Koga S, Aoki N, Uitti RJ, et al. When DLB, PD, and PSP masquerade as MSA: an autopsy study of 134 patients. *Neurology* 2015; 85: 404-12. <http://www.ncbi.nlm.nih.gov/pubmed/26138942>

Miki Y, Foti SC, Asi YT, et al Improving diagnostic accuracy of multiple system atrophy: a clinicopathological study. *Brain* 2019; 14: 2813-2827.

<https://www.ncbi.nlm.nih.gov/pubmed/31289815>

Klockgether T. The art of making a clinical diagnosis of multiple system atrophy. *Brain*. 2019; 14: 2555-2557. <https://www.ncbi.nlm.nih.gov/pubmed/31497860>

Joutsa J, Gardberg M, Røyttä M, et al. Diagnostic accuracy of parkinsonism syndromes by general neurologists. *Parkinsonism Relat Disord* 2014; 20: 840-4.

<http://www.ncbi.nlm.nih.gov/pubmed/24816002>

## MSA Useful references

Kim HJ, Stamelou M, Jeon B. Multiple system atrophy-mimicking conditions: Diagnostic challenges. *Parkinsonism Relat Disord*. 2016; 22 Suppl 1: S12-5.  
<http://www.ncbi.nlm.nih.gov/pubmed/26365777>

Gilman S, Wenning GK, Low PA, et al. Second consensus statement on the diagnosis of multiple system atrophy. *Neurology* 2008; 71: 670-6.  
<http://www.ncbi.nlm.nih.gov/pubmed/18725592>

Kollensperger M, et al. Presentations, diagnosis and management of MSA in Europe: Final analysis of the European multiple system atrophy registry. *Mov Disord* 2010; 25: 2604-12.  
<http://www.ncbi.nlm.nih.gov/pubmed/20922810>

Schrag A, et al. Cross sectional prevalence survey of idiopathic Parkinson's disease and parkinsonism in London. *Br Med J* 2000; 321: 21-22.  
<http://www.ncbi.nlm.nih.gov/pubmed/10875828>

Stankovic I, Quinn N, Vignatelli L, et al. Movement Disorder Society Multiple System Atrophy Study Group. A critique of the second consensus criteria for multiple system atrophy. *Mov Disord* 2019; 34: 975-984. <https://www.ncbi.nlm.nih.gov/pubmed/31034671>

Wenning G, et al. What clinical features are most useful to distinguish definite multiple system atrophy from Parkinson's disease? *J Neurol Neurosurg Psychiatry* 2000; 68: 434-440.  
<http://www.ncbi.nlm.nih.gov/pubmed/10727478>

Palma JA, Norcliffe-Kaufmann L, Kaufmann H. Diagnosis of multiple system atrophy. *Auton Neurosci* 2018; 211: 15-25 Review. <https://www.ncbi.nlm.nih.gov/pubmed/29111419>

Batla A, De Pablo-Fernandez E, Erro R, et al. Young-onset multiple system atrophy: Clinical and pathological features. *Mov Disord* 2018; 33: 1099-1107.  
<https://www.ncbi.nlm.nih.gov/pubmed/30153390>

Kim HJ, Jeon BS. Multiple system atrophy with prolonged survival. *Mov Disord* 2012; 27: 1834.  
<https://www.ncbi.nlm.nih.gov/pubmed/23225574>

## **Cognition**

Stankovic I, Krismer F, Jesic A, et al and Movement Disorders Society MSA (MODIMSA) Study Group. Cognitive impairment in multiple system atrophy: a position statement by the Neuropsychology Task Force of the MDS Multiple System Atrophy (MODIMSA) study group. *Lancet Neurol* 2013; 12: 264-74. <http://www.ncbi.nlm.nih.gov/pubmed/24753321>

Brown RG, Lacomblez L, Landwehrmeyer BG, et al for the NNIPPS Study Group. Cognitive impairment in patients with multiple system atrophy and progressive supranuclear palsy. *Brain* 2010; 133: 2382-93. <http://www.ncbi.nlm.nih.gov/pubmed/20576697>

Siri C, et al. A cross-sectional multicenter study of cognitive and behavioural features in multiple system atrophy patients of the parkinsonian and cerebellar type. *J Neural Transm (Vienna)* 2013; 120: 613-8. <https://www.ncbi.nlm.nih.gov/pubmed/23462799>

## MSA Useful references

Dujardin K, Defebvre L, Krystkowiak P, et al. Executive function differences in multiple system atrophy and Parkinson's disease. *Parkinsonism Relat Disord* 2003; 9: 205-11.  
<https://www.ncbi.nlm.nih.gov/pubmed/12618055>

Kawamura K, et al. Factors influencing the cognitive function in patients with multiple system atrophy. *Mov Disord* 2010; 25: 2891-2. <https://www.ncbi.nlm.nih.gov/pubmed/20925069>

Chang CC, et al. Cognitive deficits in multiple system atrophy correlate with frontal atrophy and disease duration. *Eur J Neurol* 2009; 16: 1144-50.  
<https://www.ncbi.nlm.nih.gov/pubmed/19486137>

Balas M, Balash Y, Giladi N, et al. Cognition in multiple system atrophy: neuropsychological profile and interaction with mood. *J Neural Transm (Vienna)* 2010; 117: 369-75.  
<https://www.ncbi.nlm.nih.gov/pubmed/20091064>

## **Treatment and management**

Colosimo C, Pezzella FR. The symptomatic treatment of multiple system atrophy. *Eur J Neurol* 2002; 9: 195-199. <http://www.ncbi.nlm.nih.gov/pubmed/11985626>

Kaufmann H, Freeman R, Biaggioni I, et al and NOH301 Investigators. Droxidopa for neurogenic orthostatic hypotension: a randomized, placebo-controlled, phase 3 trial. *Neurology* 2014; 83: 328-35. <http://www.ncbi.nlm.nih.gov/pubmed/24944260>

Poewe W, Mahlknecht P, Krismer F. Therapeutic advances in multiple system atrophy and progressive supranuclear palsy. *Mov Disord* 2015; 30: 1528-38 Review.  
<http://www.ncbi.nlm.nih.gov/pubmed/26227071>

Bensimon G, Ludolph A, Agid Y, et al & NNIPPS Study Group. Riluzole treatment, survival and diagnostic criteria in Parkinson plus disorders: the NNIPPS study. *Brain* 2009; 132: 156-71. <http://www.ncbi.nlm.nih.gov/pubmed/19029129>

Quinn N, Barker RA, Wenning GK. Are trials of intravascular infusions of autologous mesenchymal stem cells in patients with multiple atrophy currently justified and are they effective? *Clin Pharm Ther* 2008; 83: 663-5. <http://www.ncbi.nlm.nih.gov/pubmed/18425088>

Lee PH, Lee JE, Kim HS, et al. A randomized trial of mesenchymal stem cells in multiple system atrophy. *Ann Neurol* 2012; 72: 32-40. <http://www.ncbi.nlm.nih.gov/pubmed/22829267>

Krismer F, Poewe W, Seppi K. Comment: Autologous mesenchymal stem cells: Hope for patients with multiple system atrophy? *Neurology* 2019; 93: 25.  
<https://www.ncbi.nlm.nih.gov/pubmed/31152012>

Hussain IF, Brady CM, Swinn MJ, et al. Treatment of erectile dysfunction with sildenafil citrate (Viagra) in parkinsonism due to Parkinson's disease or multiple system atrophy with observations on orthostatic hypotension. *J Neurol Neurosurg Psychiatry* 2001; 71: 371-4.  
<http://www.ncbi.nlm.nih.gov/pubmed/11511713>

Young TM, Mathias CJ. The effects of water ingestion on orthostatic hypotension in two groups of chronic autonomic failure: multiple system atrophy and pure autonomic failure. *J Neurol Neurosurg Psychiatry* 2004; 75: 1737-41. <http://www.ncbi.nlm.nih.gov/pubmed/15548493>

## MSA Useful references

Meissner W, Laurencin C, Tranchant C, et al. Outcome of deep brain stimulation in slowly progressive multiple system atrophy: A clinico-pathological series and review of the literature. *Park Relat Disord* 2016; 24: 69-75.

<http://www.ncbi.nlm.nih.gov/pubmed/26778473>

Mathias CJ. Autonomic Diseases: Clinical features and laboratory evaluation *J Neurol Neurosurg Psychiatry* 2003; 74(Suppl 3); iii31-iii41. <http://www.ncbi.nlm.nih.gov/pubmed/12933912>

Mathias CJ. Autonomic Diseases: Management *J Neurol Neurosurg Psychiatry* 2003; 74(Suppl 3); iii42-iii47. <http://www.ncbi.nlm.nih.gov/pubmed/12933913>

Rohrer G, Höglinger GU, Levin J. Symptomatic therapy of multiple system atrophy. *Autonomic Neuroscience: Basic and Clinical* 2018; 211: 26-30.

[https://www.autonomicneuroscience.com/article/S1566-0702\(17\)30163-7/pdf](https://www.autonomicneuroscience.com/article/S1566-0702(17)30163-7/pdf)

Chelban V, Houlden H. Updates on potential therapeutic targets in MSA. *ACNR* 2016; 15: 8-11.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5870010/>

Singer W, Dietz AB, Zeller AD et al. Intrathecal administration of autologous mesenchymal stem cells in multiple system atrophy. *Neurology* 2019; 93: 77-87.

<https://www.ncbi.nlm.nih.gov/pubmed/31152011>

## **Investigations**

### **Imaging**

Umemura A, Oeda T, Hayashi R, et al. Diagnostic accuracy of apparent diffusion coefficient and <sup>123</sup>I-metaiodobenzylguanidine for differentiation of multiple system atrophy and Parkinson's disease. *PLoS One*. 2013; 8: e61066. <http://www.ncbi.nlm.nih.gov/pubmed/23613784>

Schrag A, Good CD, Miszkiet K, et al. Differentiation of atypical parkinsonian syndromes with routine MRI. *Neurology* 2000; 54: 697-702.

<http://www.ncbi.nlm.nih.gov/pubmed/10680806>

Seppi K, Schocke MF, Esterhammer R, et al. Diffusion-weighted imaging discriminates progressive supranuclear palsy from PD, but not from the parkinson variant of multiple system atrophy. *Neurology* 2003; 60: 922-7. <http://www.ncbi.nlm.nih.gov/pubmed/12654954>

Kraft E, Trenkwalder C, Auer DP. T2\*-weighted MRI differentiates multiple system atrophy from Parkinson's disease. *Neurology* 2002; 59: 1265-7.

<http://www.ncbi.nlm.nih.gov/pubmed/12391363>

Brooks DJ, Seppi K and Neuroimaging working group on MSA. Proposed neuroimaging criteria for the diagnosis of multiple system atrophy. *Mov Disord* 2009; 24: 949-64.

<http://www.ncbi.nlm.nih.gov/pubmed/19306362>

Pirker W, Asenbaum S, Bencsits G, et al. [<sup>123</sup>I]beta-CIT SPECT in multiple system atrophy, progressive supranuclear palsy, and corticobasal degeneration. *Mov Disord* 2000; 15: 1158-1167. <http://www.ncbi.nlm.nih.gov/pubmed/11104200>



## MSA Useful references

Teune LK, Bartels AL, de Jong BM, et al. Typical cerebral metabolic patterns in neurodegenerative brain diseases. *Mov Disord* 2010; 25: 2395-404.

<http://www.ncbi.nlm.nih.gov/pubmed/20669302>

Treglia G, Stefanelli A, Cason E, et al. Diagnostic performance of iodine-123-metaiodobenzylguanidine scintigraphy in differential diagnosis between Parkinson's disease and multiple-system atrophy: A systematic review and a meta-analysis. *Clin Neurol Neurosurg* 2011; 113: 823-9. <http://www.ncbi.nlm.nih.gov/pubmed/21962800>

Chelban V, Bocchetta M, Hassanein S, et al. An update on advances in magnetic resonance imaging of multiple system atrophy. *J Neurol* 2019; 266: 1036-1045.

<https://www.ncbi.nlm.nih.gov/pubmed/30460448>

Alonso-Canovas A, Tembl Ferrairo JI, Martinez-Torres I, et al. Transcranial sonography in atypical parkinsonism: How reliable is it in real clinical practice? A multicentre comprehensive study. *Parkinsonism Relat Disord* 2019; 68: 40-45 <https://www.ncbi.nlm.nih.gov/pubmed/31621617>

Paviour DC, Price SL, Jahanshahi M, et al. Longitudinal MRI in progressive supranuclear palsy and multiple system atrophy: rates and regions of atrophy. *Brain* 2016; 129: 1040-9.

<https://www.ncbi.nlm.nih.gov/pubmed/16455792>

Brenneis C, et al. Progression of brain atrophy in multiple system atrophy. A longitudinal VBM study. *J Neurol* 2007; 254: 191-6. <https://www.ncbi.nlm.nih.gov/pubmed/17334661>

Brenneis C, et al. Voxel-based morphometry detects cortical atrophy in the Parkinson variant of multiple system atrophy. *Mov Disord* 2003; 18: 1132-8.

<https://www.ncbi.nlm.nih.gov/pubmed/14534916>

Minnerop M, et al. Voxel-based morphometry and voxel-based relaxometry in multiple system atrophy-a comparison between clinical subtypes and correlations with clinical parameters. *Neuroimage* 2007; 36: 1086-95. <https://www.ncbi.nlm.nih.gov/pubmed/17512219>

Nicoletti G, Fera F, Condino F, et al. MR Imaging of Middle Cerebellar Peduncle Width: Differentiation of Multiple System Atrophy from Parkinson Disease. *Radiology* 2006; 239: 825-830.

<https://www.ncbi.nlm.nih.gov/pubmed/16714464>

Way C, Pettersson D, Hiller A. The 'Hot Cross Bun' Sign Is Not Always Multiple System Atrophy: Etiologies of 11 Cases. *Journal of Movement Disorders* 2019; 12: 27-30.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6369380/>

Brajkovic L, Kostic V, Sobic-Saranovic D, et al. The utility of FDG-PET in the differential diagnosis of Parkinsonism. *Neurological Research*, 2017; 39: 675-684.

<https://www.ncbi.nlm.nih.gov/pubmed/28378615>

Tripathi M, Dhawan V, Peng S, et al. Differential diagnosis of parkinsonian syndromes using F-18 fluorodeoxyglucose positron emission tomography. *Neuroradiology* 2013; 55: 483-492.

<https://www.ncbi.nlm.nih.gov/pubmed/23314836>

Takaya S, Sawamoto N, Okada T, et al. Differential diagnosis of parkinsonian syndromes using dopamine transporter and perfusion SPECT. *Parkinsonism & Related Disorders* 2018; 47: 15-21.

<https://www.ncbi.nlm.nih.gov/pubmed/29157745>

## **Cardiovascular autonomic features and testing**

Baschieri F, Calandra-Buonaura G, Doria A, et al. Cardiovascular autonomic testing performed with a new integrated instrumental approach is useful in differentiating MSA-P from PD at an early stage. *Parkinsonism Relat Disord*. 2015; 21: 477-82.

<http://www.ncbi.nlm.nih.gov/pubmed/25749354>

Pavy-Le Traon A, Piedvache A, Perez-Lloret S, et al and European MSA Study Group. New insights into orthostatic hypotension in multiple system atrophy: a European multicentre cohort study. *J Neurol Neurosurg Psychiatry* 2016; 87: 554-561.

<http://www.ncbi.nlm.nih.gov/pubmed/25977316>

Riley DE, Chelimsky TC. Autonomic nervous system testing may not distinguish multiple system atrophy from Parkinson's disease. *J Neurol Neurosurg Psychiatry* 2003; 74: 56-60.

<http://www.ncbi.nlm.nih.gov/pubmed/12486267>

Reimann M, Schmidt C, Herting B, et al. Comprehensive autonomic assessment does not differentiate between Parkinson's disease, multiple system atrophy and progressive supranuclear palsy. *J Neural Transm* 2010; 117: 69-76. <http://www.ncbi.nlm.nih.gov/pubmed/19763772>

Giannini G, Calandra-Buonaura G, Asioli GM, et al. The natural history of idiopathic autonomic failure: The IAF-BO cohort study. *Neurology* 2018; 91: 1245-1254.

<https://www.ncbi.nlm.nih.gov/pubmed/30135257>

Iodice, V, et al. Autopsy confirmed multiple system atrophy cases: Mayo experience and role of autonomic function tests. *J Neurol Neurosurg Psychiatry* 2012; 83: 453-9.

<https://www.ncbi.nlm.nih.gov/pubmed/22228725>

## **Urogenital features and testing**

Kirchhof K, Apostolidis AN, Mathias CJ, et al. Erectile and urinary dysfunction may be the presenting features in patients with multiple system atrophy: a retrospective study. *Int J Impot Res* 2003; 15: 293-8. <http://www.ncbi.nlm.nih.gov/pubmed/12934060>

Sakakibara R, Uchiyama T, Yamanishi T, et al. Sphincter EMG as a diagnostic tool in autonomic disorders. *Clin Auton Res* 2009; 19: 20-31 Review. <http://www.ncbi.nlm.nih.gov/pubmed/18780143>

Beck R, Betts C, Fowler C. Genitourinary dysfunction in multiple system atrophy: clinical features and treatment in 62 cases. *J Urol* 1994; 151: 1336-41.

<http://www.ncbi.nlm.nih.gov/pubmed/8158782>

Paviour DC, Williams D, Fowler CJ, et al. Is sphincter electromyography a helpful investigation in the diagnosis of multiple system atrophy? A retrospective study with pathological diagnosis. *Mov Disord* 2005; 20: 1425-30.

<http://www.ncbi.nlm.nih.gov/pubmed/16007638>

Oertel WH, Wachter T, Quinn NP, et al. Reduced genital sensitivity in female patients with multiple system atrophy of parkinsonian type. *Mov Disord* 2002; 18: 430-432.

<http://www.ncbi.nlm.nih.gov/pubmed/12671951>

## MSA Useful references

Uchiyama T, Sakakibara R, Asahina M, et al. Post-micturitional hypotension in patients with multiple system atrophy. *J Neurol Neurosurg Psychiatry* 2005; 76: 186-190.  
<http://www.ncbi.nlm.nih.gov/pubmed/15654029>

Panicker JN, Simeoni S, Miki Y, et al. Early presentation of urinary retention in multiple system atrophy: can the disease begin in the sacral spinal cord? *J Neurol* 2020; 267: 659-664 PMID: 31720822 <https://www.ncbi.nlm.nih.gov/pubmed/31720822>

Fanciulli A, Goebel G, Lazzeri G, et al. Urinary retention discriminates multiple system atrophy from Parkinson's disease. *Mov Disord* 2019; 34: 1926-1928.  
<https://www.ncbi.nlm.nih.gov/pubmed/31710392>

Sakakibara R, et al. Bladder dysfunction as the initial presentation of multiple system atrophy: a prospective cohort study. *Clin Auton Res* 2019; 29: 627-631.  
<https://www.ncbi.nlm.nih.gov/pubmed/30043182>

Yamamoto T, et al. The Utility of Post-Void Residual Volume versus Sphincter Electromyography to Distinguish between Multiple System Atrophy and Parkinson's Disease. *PLoS One* 2017; 12, e0169405. <https://www.ncbi.nlm.nih.gov/pubmed/28060892>

### **Other clinical features**

Anderson T, Luxon L, Quinn N, et al Oculomotor function in multiple system atrophy: clinical and laboratory features in 30 patients. *Mov Disord* 2008; 23: 977-84.  
<http://www.ncbi.nlm.nih.gov/pubmed/18383533>

Salazar G, Valls-Solé J, Martí MJ, et al. Postural and action myoclonus in patients with parkinsonian type multiple system atrophy. *Mov Disord* 2000; 15: 77-83.  
<http://www.ncbi.nlm.nih.gov/pubmed/10634245>

Klein C, Brown R, Wenning G, et al. The “cold hands sign” in multiple system atrophy. *Mov Disord* 1997; 4: 514-8. <http://www.ncbi.nlm.nih.gov/pubmed/9251069>

Santens P, Crevits L, Van der Linden C. Raynaud's phenomenon in a case of multiple system atrophy. *Mov Disord* 1996; 5: 586-8. <http://www.ncbi.nlm.nih.gov/pubmed/8866508>

Boesch SM, Wenning GK, Ransmayr G, et al. Dystonia in multiple system atrophy. *J Neurol Neurosurg Psychiatry* 2002; 72: 300-303. <http://www.ncbi.nlm.nih.gov/pubmed/11861684>

Wenning GK, Geser F, Poewe W. The “risus sardonicus” of multiple system atrophy. *Mov Disord* 2003; 10: 1211. <http://www.ncbi.nlm.nih.gov/pubmed/14534935>

Quinn N. Disproportionate antecollis in multiple system atrophy. *Lancet* 1989; 1: 844.  
<http://www.ncbi.nlm.nih.gov/pubmed/2564927>

Colosimo C. Pisa syndrome in a patient with multiple system atrophy. *Mov Disord* 1998; 3: 607-9. <http://www.ncbi.nlm.nih.gov/pubmed/9613765>

Kollensperger M, Geser F, Seppi K, et al. Red flags for multiple system atrophy. *Mov Disord* 2008; 23: 1093-9 <http://www.ncbi.nlm.nih.gov/pubmed/18442131>

Gurevich T, Giladi N. Freezing of gait in multiple system atrophy (MSA). *Parkinsonism Relat Disord* 2003; 9: 169-174. <http://www.ncbi.nlm.nih.gov/pubmed/12573873>



## MSA Useful references

Kluin KJ, Gilman S, Lohnman, et al. Characteristics of the Dysarthria of Multiple System Atrophy. Arch Neurol 1996; 53: 545-458. <http://www.ncbi.nlm.nih.gov/pubmed/8660157>

Hughes T. Neurology of swallowing and oral feeding disorders: assessment and management. J Neurol Neurosurg Psychiatry 2003; 74 (Suppl III): iii48-iii52. <http://www.ncbi.nlm.nih.gov/pubmed/12933914>

Cortelli P, Calandra-Buonaura G, Benarroch EE, et al. Stridor in multiple system atrophy: Consensus statement on diagnosis, prognosis, and treatment. Neurology 2019; 93: 630-639 PMID: 31570638 <https://www.ncbi.nlm.nih.gov/pubmed/31570638>

Fanciulli A, Goebel G, Lazzeri G, et al. Early distinction of Parkinson-variant multiple system atrophy from Parkinson's disease. Mov Disord 2019; 34: 440-441. PMID: 30788854 <https://www.ncbi.nlm.nih.gov/pubmed/30788854>

Bhidayasiri R, Sringean J, Reich SG, et al. Red flags phenotyping: A systematic review on clinical features in atypical parkinsonian disorders. Parkinsonism Relat Disord 2019; 59: 82-92 PMID: 30409560 <https://www.ncbi.nlm.nih.gov/pubmed/30409560>

Silber MH, Levine S. Stridor and death in multiple system atrophy. Mov Disord 2000; 15: 699-704. <https://www.ncbi.nlm.nih.gov/pubmed/10928581>

Colosimo C. Nonmotor presentations of multiple system atrophy. Nat Rev Neurol 2011; 7: 295-8. <https://www.ncbi.nlm.nih.gov/pubmed/21343894>

Coon EA, et al. Anhidrosis in multiple system atrophy involves pre- and postganglionic sudomotor dysfunction. Mov Disord 2017; 32: 397-404. <https://www.ncbi.nlm.nih.gov/pubmed/27859565>

Parvizi J, et al. Diagnosis and management of pathological laughter and crying. Mayo Clin Proc 2006; 81: 1482-6. <https://www.ncbi.nlm.nih.gov/pubmed/17120404>

Parvizi J, Joseph J, Press DZ, et al. Pathological laughter and crying in patients with multiple system atrophy-cerebellar type. Mov Disord 2007; 22: 798-803. <https://www.ncbi.nlm.nih.gov/pubmed/17290465>

Benrud-Larson LM, Sandroni P, Schrag A, et al. Depressive symptoms and life satisfaction in patients with multiple system atrophy. Mov Disord 2005; 20: 951-7. <https://www.ncbi.nlm.nih.gov/pubmed/15782421>

Schrag A, et al. Health-related quality of life in multiple system atrophy. Mov Disord 2006; 21: 809-15. <https://www.ncbi.nlm.nih.gov/pubmed/16502399>

Schrag A, et al. A comparison of depression, anxiety, and health status in patients with progressive supranuclear palsy and multiple system atrophy. Mov Disord 2010; 25: 1077-81. <https://www.ncbi.nlm.nih.gov/pubmed/20535826>

## MSA Useful references

Armstrong RA. Visual signs and symptoms of multiple system atrophy. Clin Exp Optom 2014; 97: 483-91. <https://www.ncbi.nlm.nih.gov/pubmed/25256122>

### **Sleep**

Cormican LJ, Higgins S, Davidson AC, et al. Multiple system atrophy presenting as central sleep apnoea. Eur Resp J 2004; 24: 323-325. <http://www.ncbi.nlm.nih.gov/pubmed/15332405>

Ghorayeb I, Yekhlief V, Chryatostome, V, et al. Sleep disorders and their determinants in multiple system atrophy. J Neurol Neurosurg Psychiatry 2002; 72: 798-800. <http://www.ncbi.nlm.nih.gov/pubmed/12023429>

Iranzo A, et al. Long-term effect of CPAP in the treatment of nocturnal stridor in multiple system atrophy. Neurology 2004; 63: 930-932. <http://www.ncbi.nlm.nih.gov/pubmed/15365155>

Plazzi G, Corsini R, Provini F, et al. REM sleep behavior disorders in multiple system atrophy. Neurology 1997; 48: 1094-7. <http://www.ncbi.nlm.nih.gov/pubmed/9109907>

Muntean ML, Sixel-Doring F, Trenkwalder C. No Difference in Sleep and RBD between Different Types of Patients with Multiple System Atrophy: A Pilot Video-Polysomnographical Study. Sleep Disord 2013; 258390. <https://www.ncbi.nlm.nih.gov/pubmed/23766915>

Palma JA, et al. Prevalence of REM sleep behavior disorder in multiple system atrophy: a multicenter study and meta-analysis. Clin Auton Res 2015; 25: 69-75. <https://www.ncbi.nlm.nih.gov/pubmed/25739474>

Ohshima Y, et al. Natural course and potential prognostic factors for sleep-disordered breathing in multiple system atrophy. Sleep Med 2017; 34: 13-17. <https://www.ncbi.nlm.nih.gov/pubmed/28522081>

### **MSA-C**

Teive HA, Arruda WO, Moro A, et al. Differential diagnosis of sporadic adult-onset ataxia: The role of REM sleep behavior disorder. Parkinsonism Relat Disord 2015; 21: 640-3. <http://www.ncbi.nlm.nih.gov/pubmed/25899546>

Lin DJ, Hermann KL, Schmahmann JD. Multiple system atrophy of the cerebellar type: Clinical state of the art. Mov Disord 2014; 29: 294-304. <http://www.ncbi.nlm.nih.gov/pubmed/24615754>

Klockgether T. Sporadic ataxia with adult onset: classification and diagnostic criteria. Lancet Neurol 2010; 9: 94-104. <http://www.ncbi.nlm.nih.gov/pubmed/20083040>

Watanabe H, Saito Y, Terao S, et al. Progression and prognosis in multiple system atrophy. An analysis of 230 Japanese patients. Brain 2002; 125: 1070-1083. <http://www.ncbi.nlm.nih.gov/pubmed/11960896>

## **Pathology & Alpha-synuclein**

Papp M, Kahn JE, Lantos PL. Glial cytoplasmic inclusions in the CNS of patients with multiple system atrophy (striatonigral degeneration, olivopontocerebellar atrophy and Shy Drager syndrome). *J Neurol Sci* 1989; 94: 79-100. <http://www.ncbi.nlm.nih.gov/pubmed/2559165>

Burn DJ, Jaros E. Multiple system atrophy: cellular and molecular pathology. *J Clin Path* 2001; 54: 419-426. <http://www.ncbi.nlm.nih.gov/pubmed/11724918>

Peelaerts W, Bousset L, Van der Perren A, et al.  $\alpha$ -Synuclein strains cause distinct synucleinopathies after local and systemic administration. *Nature* 2015; 522: 340-4. <http://www.ncbi.nlm.nih.gov/pubmed/26061766>

Woerman AL, Watts JC, Aoyagi A, et al.  $\alpha$ -Synuclein: Multiple System Atrophy Prions. *Cold Spring Harb Perspect Med* 2018 Jul 2; 8(7). <https://www.ncbi.nlm.nih.gov/pubmed/28213437>

Prusiner SB, Woerman AL, Mordes DA, et al. Evidence for  $\alpha$ -synuclein prions causing multiple system atrophy in humans with parkinsonism. *Proc Natl Acad Sci USA* 2015; 112(38): E5308-17. <http://www.ncbi.nlm.nih.gov/pubmed/26324905>

Wakabayashi K, Yoshimoto M, Tsuji S, et al. Alpha-synuclein immunoreactivity in glial cytoplasmic inclusions in multiple system atrophy. *Neurosci Lett* 1998; 249: 180-2. <http://www.ncbi.nlm.nih.gov/pubmed/9682846>

Kiely AP, Asi YT, Kara E, et al. Alpha-synucleinopathy associated with G51D SNCA mutation: A link between Parkinson's disease and multiple system atrophy? *Acta Neuropathol* 2013; 125: 753-69. <http://www.ncbi.nlm.nih.gov/pubmed/23404372>

Wenning G, Jellinger KA. The role of alpha-synuclein in the pathogenesis of multiple system atrophy. *Acta Neuropathol* 2005; 109: 129-40. <http://www.ncbi.nlm.nih.gov/pubmed/15666181>

Shahnawaz M, Mukherjee A, Pritzkow S et al Discriminating  $\alpha$ -synuclein strains in Parkinson's disease and multiple system atrophy. *Nature* 2020; 578: 273-277. <https://www.ncbi.nlm.nih.gov/pubmed/32025029>

Heras-Garvin A, Weckbecker D, Ryazanov S, et al. Anle138b modulates  $\alpha$ -synuclein oligomerization and prevents motor decline and neurodegeneration in a mouse model of multiple system atrophy. 2019; 34: 255-263. <https://www.ncbi.nlm.nih.gov/pubmed/30452793>

Stefanova N, et al. Microglial activation mediates neurodegeneration related to oligodendroglial alpha-synucleinopathy: implications for multiple system atrophy. *Mov Disord* 2007; 22: 2196-203. <https://www.ncbi.nlm.nih.gov/pubmed/17853477>

Wakabayashi K, et al. An autopsy case of early ("minimal change") olivopontocerebellar atrophy (multiple system atrophy-cerebellar). *Acta Neuropathol* 2005; 110: 185-90. [https://www.researchgate.net/publication/7772486\\_An\\_autopsy\\_case\\_of\\_early\\_minimal\\_change\\_olivopontocerebellar\\_atrophy\\_multiple\\_system\\_atrophy-cerebellar](https://www.researchgate.net/publication/7772486_An_autopsy_case_of_early_minimal_change_olivopontocerebellar_atrophy_multiple_system_atrophy-cerebellar)

## **Reviews and History**

Fanciulli A, Wenning GK. Multiple system atrophy. *N Engl J Med* 2015; 372: 249-63 Review. <http://www.ncbi.nlm.nih.gov/pubmed/25587949>

## MSA Useful references

Quinn N. A short clinical history of multiple system atrophy. *Clin Aut Res* 2015; 25: 3-7. <http://www.ncbi.nlm.nih.gov/pubmed/25578151>

Quinn N. Multiple system atrophy--the nature of the beast. *J Neurol Neurosurg Psychiatry* 1989; 52 (suppl): 78-89. <http://www.ncbi.nlm.nih.gov/pubmed/2666581>

Quinn N. Multiple system atrophy: the nature of the beast revisited. *J Neurol Neurosurg Psychiatry* 2020; 91: 3-4. <https://www.ncbi.nlm.nih.gov/pubmed/31848228>

Stefanova N, Bucke P, Duerr S, et al. Multiple system atrophy: an update. *Lancet Neurol* 2009; 8: 1172-8. <http://www.ncbi.nlm.nih.gov/pubmed/19909915>

Fanciulli A, Stankovic I, Krismer F, et al. Multiple system atrophy. *Int Rev Neurobiol* 2019; 149: 137-192. <https://www.ncbi.nlm.nih.gov/pubmed/31779811>

Meissner WG, Fernagut PO, Dehay B, et al. Multiple System Atrophy: Recent Developments and Future Perspectives. *Mov Disord*. 2019; 34: 1629-1642 Review. <https://www.ncbi.nlm.nih.gov/pubmed/31692132>

Watanabe H, Riku Y, Hara K, et al. Clinical and imaging features of multiple system atrophy: Challenges for an early and clinically definitive diagnosis. *J Mov Disord* 2018; 11: 107-120 <https://www.ncbi.nlm.nih.gov/pubmed/30086614>

Jellinger KA, Wenning GK. Multiple system atrophy: pathogenic mechanisms and biomarkers. *J Neural Transm (Vienna)* 2016; 123: 555-72. <https://www.ncbi.nlm.nih.gov/pubmed/27098666>

Ben-Shlomo Y, Wenning GK, Tison F, et al. Survival of patients with pathologically proven multiple system atrophy: a meta-analysis. *Neurology* 1997; 48: 384-93. <https://www.ncbi.nlm.nih.gov/pubmed/9040727>

Krismer F, Wenning GK. Multiple system atrophy: insights into a rare and debilitating movement disorder. *Nat Rev Neurol* 2017; 13: 232-243. <https://www.ncbi.nlm.nih.gov/pubmed/28303913>

Jecmenica-Lukic M, Poewe W, Tolosa, E, et al. Premotor signs and symptoms of multiple system atrophy. *Lancet Neurol* 2012; 11: 361-8. <https://www.ncbi.nlm.nih.gov/pubmed/22441197>

## **Genetics**

Sailer A, Scholz SW, Nalls MA, et al and the EMSA & UK MSA Study Groups. A genome-wide association study in Multiple System Atrophy (MSA). 2016; 87: 1591-1598. <http://www.emsa-sg.org/index.php?id=128>

Sturm E, Stefanova N. Multiple System Atrophy: Genetic or Epigenetic?. *Experimental Neurobiology* 2014; 23: 277. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4276800/>

Kim HJ, Jeon BS, Shin J, et al. Should genetic testing for SCAs be included in the diagnostic workup for MSA? *Neurology* 2014; 83: 1733–1738. <https://www.ncbi.nlm.nih.gov/pubmed/25298309>

Hara K, Momose Y, Tokiguchi S, et al. Multiplex Families With Multiple System Atrophy. *Arch Neurol* 2007; 64: 545–551. <https://www.ncbi.nlm.nih.gov/pubmed/17420317>

## MSA Useful references

Scholz SW, Houlden H, Schulte C, et al. SNCA variants are associated with increased risk for multiple system atrophy. *Annals of neurology* 2019; 5: 610-4.

<https://europepmc.org/article/pmc/pmc4727743>

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