

SPLICING

CNS involvement in DM1 is driven by spliceopathy (dysregulated alternative splicing in the brain)¹⁻³



Numerous genes show missplicing in DM1 brain autopsy samples and animal models, including *MAPT* (tau protein) and *NMDAR1* (NMDA synaptic receptor protein)^{1,4}

STRUCTURAL CHANGES

Several pathologic changes occur in the brain; however, the process of how the molecular pathophysiology of DM1 leads to structural brain changes in DM1 has yet to be fully elucidated⁵⁻⁷

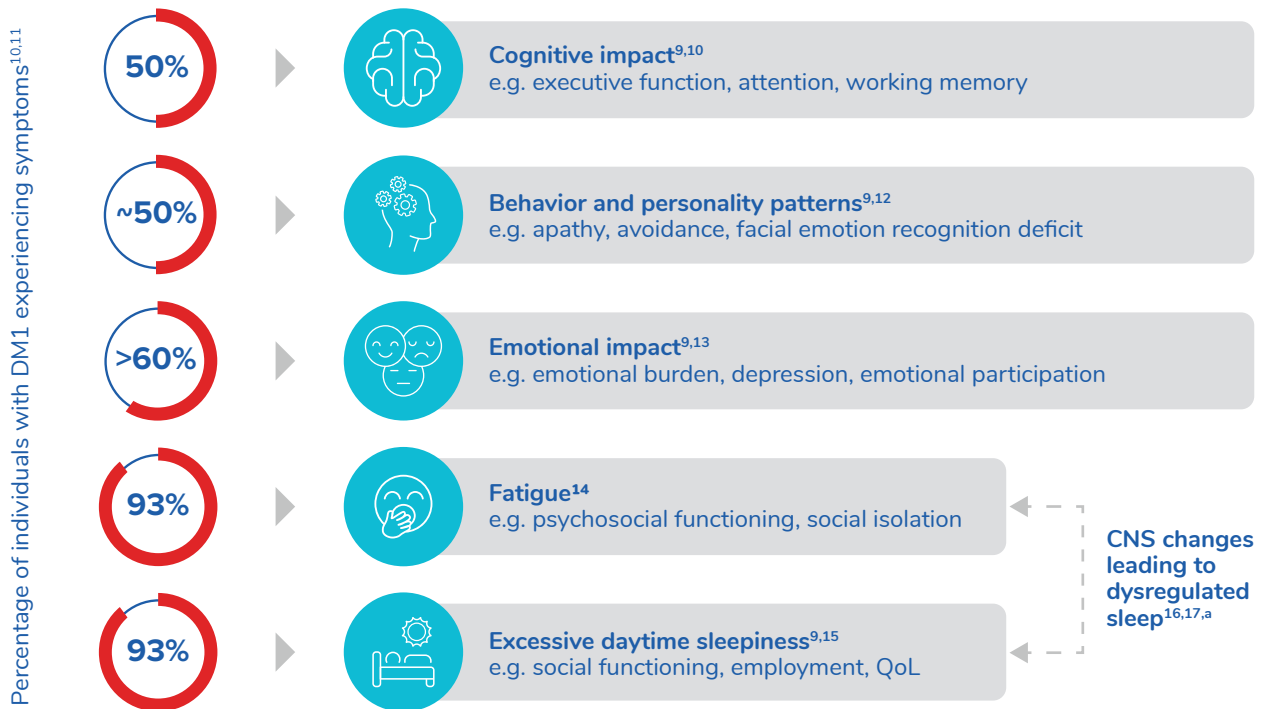
Protein and nucleotide deposits

Cellular alterations

Structural alterations

CLINICAL MANIFESTATIONS

Almost every individual with DM1 experiences some form of CNS involvement, yet symptoms are heterogeneous, spanning a range of neuropsychological aspects^{8,9}



DM1 symptoms with a CNS component negatively impact relationships, social interactions, employment and other aspects of the lives of individuals living with DM1^{8,9,11,18}

Footnotes: ^aSleep-related symptoms in DM1 are driven by complex interactions between many factors, with sleep disordered breathing, primary CNS dysfunction, and muscle weakness all playing a role.
Abbreviations: CNS, central nervous system; DM1, myotonic dystrophy type 1; QoL, quality of life.

References: 1. López-Martínez A, et al. *Genes (Basel)*. 2020;11(9):1109; 2. Nakamori M, et al. *Brain Commun*. 2022;4(3):fcac154; 3. Liu J, et al. *Front Aging Neurosci*. 2021;13:755392; 4. Charizanis K, et al. *Neuron*. 2012;75(3):437–450; 5. Weijs R, et al. *Neuropathology*. 2021;41(1):3–20; 6. Schneider-Gold C, et al. *PLoS One*. 2015;10(6):e0130352; 7. van der Plas E, et al. *J Neuromuscul Dis*. 2019;6(3):321–332; 8. Wenninger S, et al. *Front Neurol*. 2018;9:303; 9. Meola G & Sansone V. *Muscle Nerve*. 2007;36:294–306; 10. Fujino H, et al. *Muscle Nerve*. 2018;57(5):742–748; 11. Hagerman KA, et al. *Muscle Nerve*. 2019;59:457–464; 12. Winblad S, et al. *J Neurol Neurosurg Psychiatry*. 2006;77(2):219–223; 13. Minier L, et al. *J Neuromuscul Dis*. 2018;5(3):279–294; 14. Winblad S & Lindberg C. *BMC Neurol*. 2019;19(1):45; 15. Laberge L, et al. *Curr Neurol Neurosci Rep*. 2013;13(4):340; 16. Subramony SH, et al. *Muscle Nerve*. 2020;62(3):309–320; 17. Hamilton MJ, et al. *Neuromuscul Disord*. 2022;32(5):377–389; 18. Heatwole C, et al. *Neurology*. 2012;79(4):348–357.