Understanding how DM1 affects the brain

With this interactive module, you can learn how DM1 impacts the brain and understand the burden of disease across the key domains of cognition, behavior and emotion, and fatigue and excessive daytime sleepiness.

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Which topic would you like to explore first?

Pathophysiology

Cognition

Personality and emotion

Fatigue and EDS

EDS, excessive daytime sleepiness.

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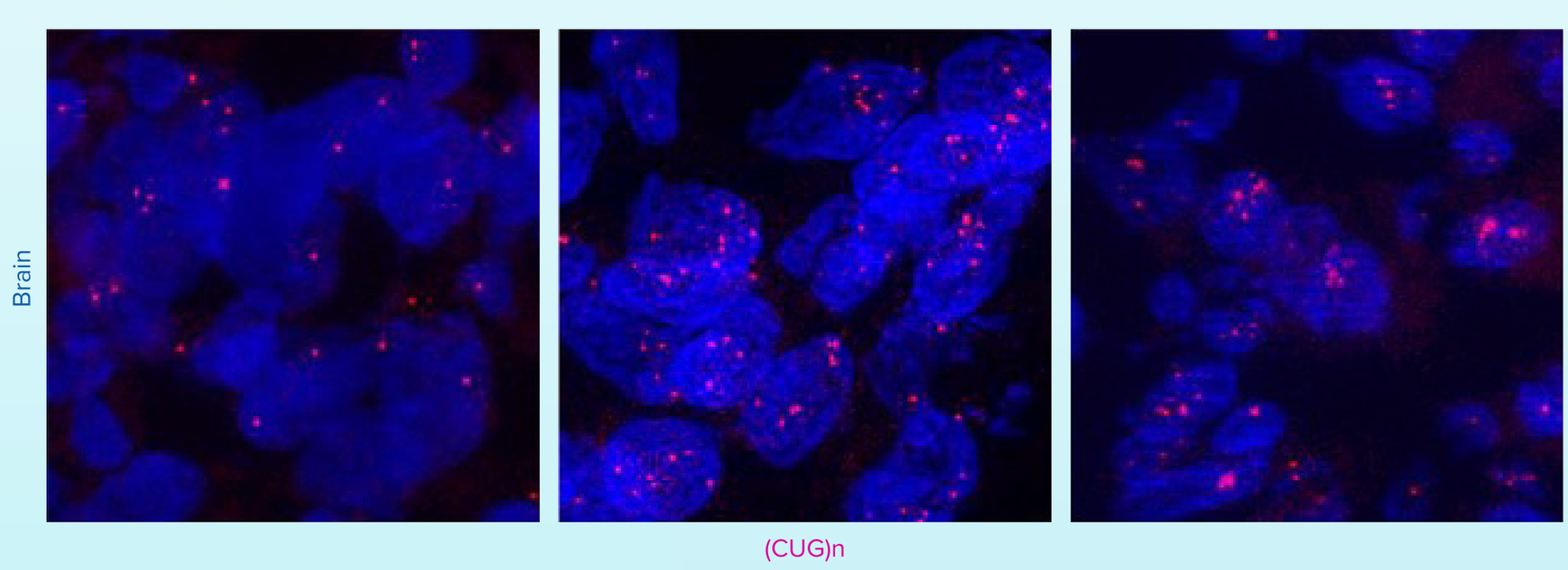
PATHOPHYSIOLOGY

Introduction

CNS involvement in DM1 is driven by spliceopathy (dysregulated gene transcript splicing) in the brain[1–3]

Mutant *DMPK* mRNA forms a hairpin structure that sequesters MBNL splicing factors into toxic nuclear foci. The sequestration of MBNL splicing factors dysregulates gene transcript splicing in multiple tissues, which drives the multisystemic disease manifestations of DM1, including those in the CNS[1]



Toxic nuclear foci accumulate in DM1 tissues during fetal development[4]

The toxic nuclear foci in DM1 appear as visible histopathologic alterations that are directly linked to missplicing in the brain[5]

Tap to learn more about which genes are known to be misspliced in the brain

NEXT

CNS, central nervous system; **CUG,** cytosine-uracil-guanine; **DM1,** myotonic dystrophy type 1; **DMPK,** dystrophia myotonica protein kinase; **MBNL,** muscleblind-like; **mRNA,** messenger ribonucleic acid.

Image reference: Michel L, et al. *PLoS One.* 2015;10(9):e0137620. Licensed under a CC-BY 4.0 Creative Commons license.

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. Michel L, et al. *PLoS One.* 2015;10(9):e0137620; 5. Weijs R, et al. *Neuropathology.* 2021;41(1):3–20.

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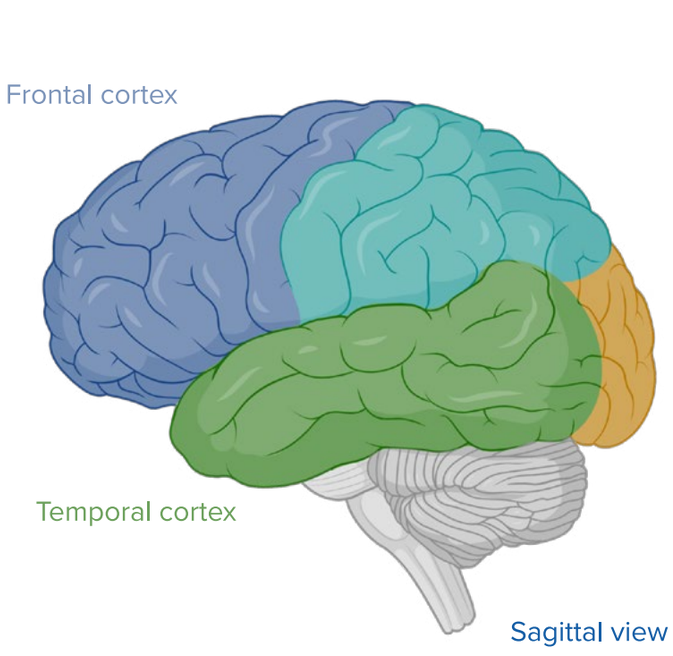
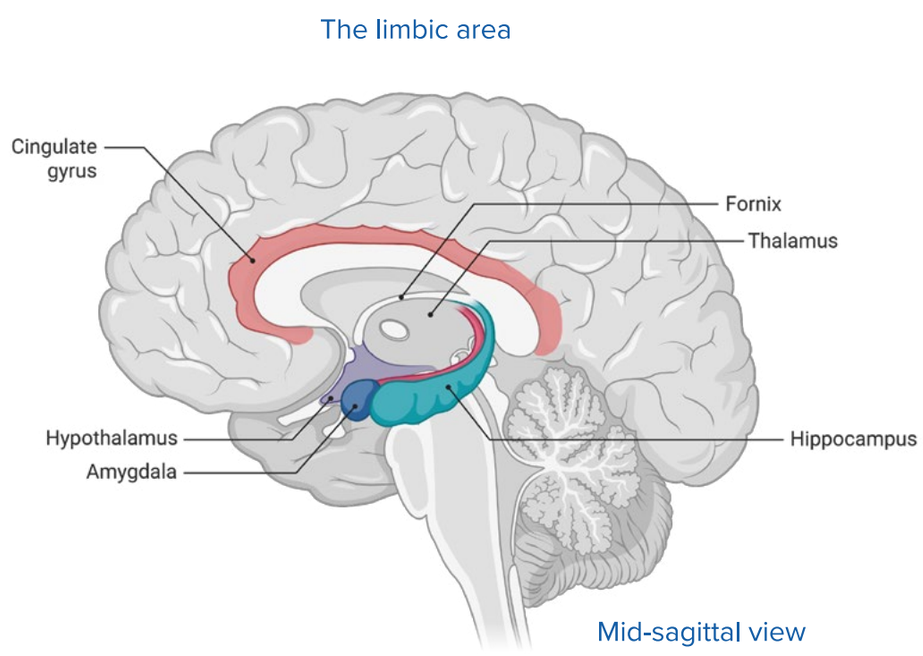
Misspliced transcripts





Human brain tissue samples

Misspliced gene	Brain region	Gene function*	Potential CNS pathology*
MAPT[1,2]	Frontal cortex Limbic area	Tau protein	Primary age-related tauopathy (PART)-like degeneration of brain tissue
NMDAR1[3–5]	Temporal cortex	Synaptic transmission and plasticity	Learning and memory
GRIP1[1]	Frontal cortex	Synaptic scaffolding	Reduced synaptic plasticity
DLGAP1[1,6]	Frontal cortex	Synaptic scaffolding	Altered synaptic transmission
KCNMA1[1,7,8]	Frontal cortex Temporal cortex	Ion channel function	Altered neuronal activity
CSNK1D[1,7,9]	Frontal cortex Temporal cortex	Kinase	Circadian rhythm disruption
GARBG2[1,10]	Frontal cortex	Neurotransmitter receptor	Dysregulation of GABA sensitivity

*Some gene functions and potential CNS pathology are based on animal models

Proteomic analysis of CSF samples from individuals with DM1 support transcriptomic findings that diverse pathways may underlie CNS dysfunction[11]

GABA, gamma-aminobutyric acid.

Figures from BioRender.

References: 1. Otero BA, et al. *Cell Rep.* 2021;34:108634; 2. Hamasaki H, et al. *J Neuropathol Exp Neurol.* 2022;82(1):29–37; 3. López-Martínez A, et al. *Genes (Basel).* 2020;11(9):1109; 4. Jiang H, et al. *Hum Mol Genet.* 2004;13(24):3079–3088; 5. Jewett BE, Thapa B. Physiology, NMDA Receptor. [Updated 2022 Dec 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK519495/; 6. NIH National Library of Medicine. DLGAP1 DLG associated protein 1. Available from: https://www.ncbi.nlm.nih.gov/gene/9229. Accessed January 2026; 7. Charizanis K, et al. *Neuron.* 2012;75(3):437–450; 8. Bailey CS, et al. *J Gen Physiol.* 2019;151(10):1173–1189; 9. Eng GWL, et al. *PLoS One.* 2017;12(5):e0177834; 10. Edokpolor KS, et al. *eNeuro.* 2022;9(5):ENEURO.0218–22.2022; 11. Zafarulla M, et al. *Front Neurosci.* 2025;19:1709678.

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PATHOPHYSIOLOGY

Spliceopathy

Several pathologic changes occur in the brain downstream of spliceopathy[1,2]

Protein and nucleotide deposits[1]

Cellular alterations[1]

Structural alterations[1,3]
(Tap to learn more)

Many neuropathologic features of DM1 resemble those found in other neurodegenerative diseases and can also be seen to some extent in the normal aging process[1]

The process of how the molecular pathophysiology of DM1 leads to structural brain changes in DM1 has yet to be fully elucidated[4]

NEXT

DM1, myotonic dystrophy type 1.

References: 1. Weijs R, et al. *Neuropathology.* 2021;41(1):3-20; 2. Yoshizumi K, et al. *Neurosci Res.* 2024;200:48-56;
3. Schneider-Gold C, et al. *PLoS One.* 2015; 10(6):e0130352;
4. van der Plas E, et al. *J Neuromuscul Dis.* 2019;6(3):321–332.

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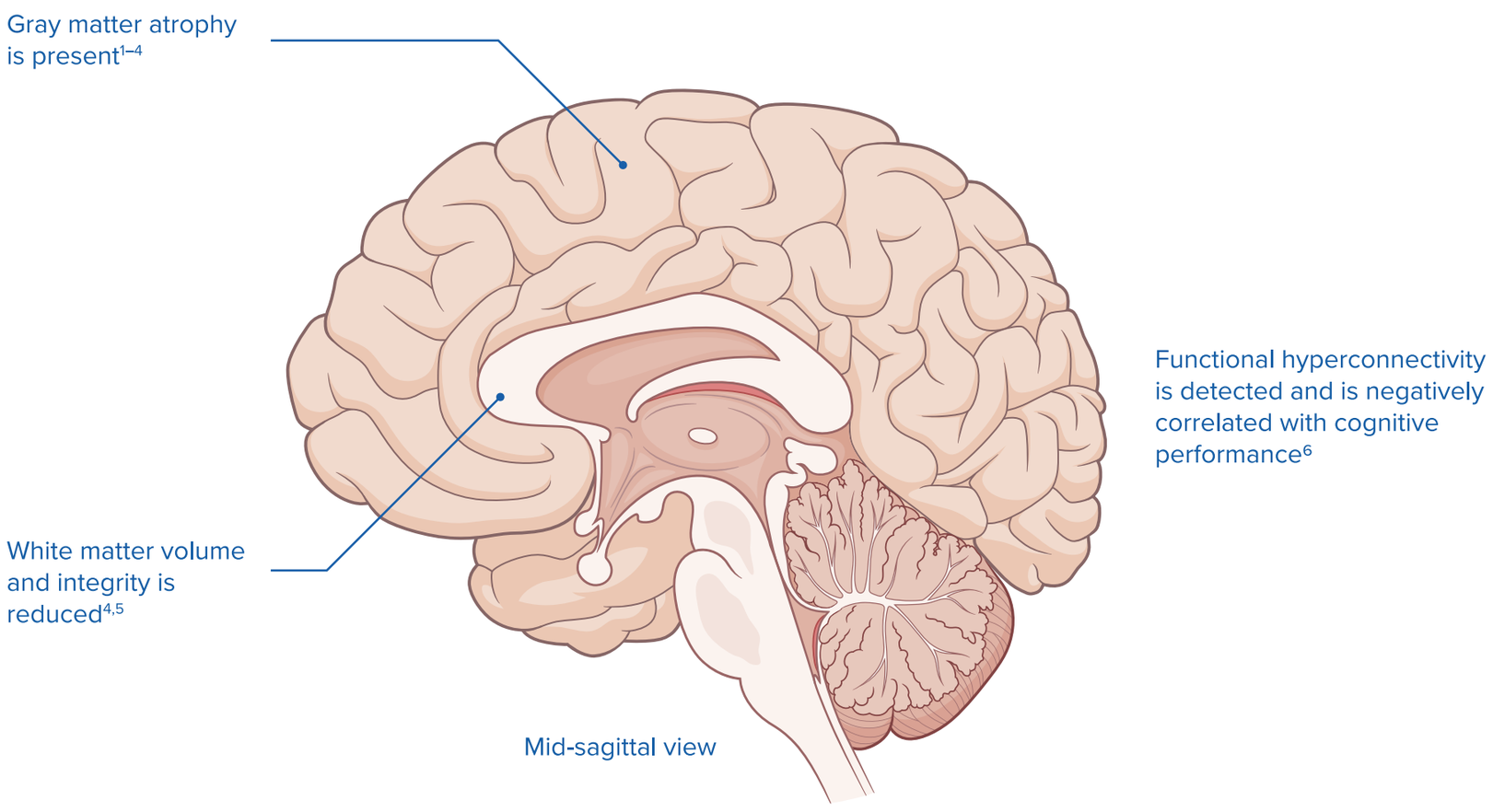
Structural and functional alterations



Gray matter atrophy is negatively associated with cognitive impairments*[2–4]

- Recall[3]
- Flexibility of thinking[2]
- Visuoconstruction[4]
- Executive performance[4]

White matter abnormalities are associated with cognitive impairments*[1,7]

- Working memory[1,7]
- Reason and problem solving[1]
- Visuospatial[1]

Hyperconnectivity negatively correlates with estimated IQ, visuoconstruction, and executive function domains[6]

Occipital lobe and amygdala volumes are associated with sleep architecture alterations. Hippocampus volume is associated with EDS symptoms[8]

*List is not exhaustive

DM1, myotonic dystrophy type 1; **EDS,** excessive daytime sleepiness; **IQ,** intelligence quotient.

References: 1. Caso F, et al. *PLoS One.* 2014; 9(8):e104697; 2. Schneider-Gold C, et al. *PLoS One.* 2015; 10(6):e0130352; 3. Jiang Q, et al. *Front Neurol.* 2022;13:891789; 4. Labayru G, et al. *Neuroimage Clin.* 2019;24:102078; 5. Labayru G, et al. *SciRep.* 2022;12:3988; 6. Garmendia J, et al. *J Neuromuscul Dis.* 2025;12(1):90–101; 7. Cabada T, et al. *Neuroradiology.* 2021;63(7):1019–1029; 8. Hamilton MJ, et al. *Neuromuscul Disord.* 2022;32(5):377–389.

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PATHOPHYSIOLOGY

The direct impact of DM1 on the brain

Almost every individual with DM1 experiences some form of CNS involvement, yet symptoms are heterogeneous[1,2]

CNS involvement in DM1 can impact five key domains in affected individuals[2]

Some symptoms with a CNS component can have a greater impact on individuals living with DM1 than some muscular symptoms, yet CNS-driven symptoms can be under-appreciated by clinicians and individuals living with DM1[1,5–8]

SELECT TOPIC

CNS, central nervous system; **EDS,** excessive daytime sleepiness; **DM1,** myotonic dystrophy type 1.

References: 1. Wenninger S, et al. *Front Neurol.* 2018;9:303; 2. Meola G & Sansone V. *Muscle Nerve.* 2007;36: 294–306; 3. Subramony SH, et al. *Muscle Nerve.* 2020;62:309–320; 4. Hamilton MJ, et al. *Neuromuscul Disord.* 2022;32(5):377–389; 5. Hagerman KA, et al, *Muscle Nerve.* 2019;59:457–464; 6. Heatwole C, et al. *Neurology.* 2012;79(4):348–357; 7. Simoncini C, et al. *Front Neurol.* 2020;11:624; 8. Baldanzi S, et al. *Orphanet J Rare Dis.* 2016;11:34.

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CNS symptoms negatively impact relationships, social interactions, employment and other aspects of the lives of individuals living with DM1[1–5]

Cognitive impact[1,6]
e.g. executive function, attention, working memory

Behavior/personality patterns[1,7]
e.g. apathy, avoidance, facial emotion recognition deficit

Emotional impact[1,3]
e.g. emotional burden, depression, emotional participation

Fatigue[2]
e.g. psychosocial functioning, social isolation

Excessive daytime sleepiness[1,5]
e.g. social functioning, employment, QoL

CNS, central nervous system; **DM1,** myotonic dystrophy type 1; **QoL,** quality of life.

References: 1. Meola G & Sansone V. *Muscle Nerve.* 2007;36: 294–306; 2. Winblad S & Lindberg C. *BMC Neurol.* 2019;19(1):45; 3. Minier L, et al. *J Neuromuscul Dis.* 2018;5(3):279–294; 4. Hagerman KA, et al. *Muscle Nerve.* 2019;59(4):457–464; 5. Laberge L, et al. *Curr Neurol Neurosci Rep.* 2013;13(4):340; 6. Fujino H, et al. *Muscle Nerve.* 2018;57(5):742–748; 7. Winblad S, et al. *J Neurol Neurosurg Psychiatry.* 2006;77(2):219–23.

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COGNITION

TRUE OR FALSE?

Cognitive involvement is only present in congenital/childhood-onset DM1

TRUE

FALSE

DM1, myotonic dystrophy type 1.

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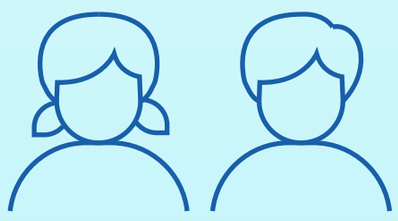
COGNITION

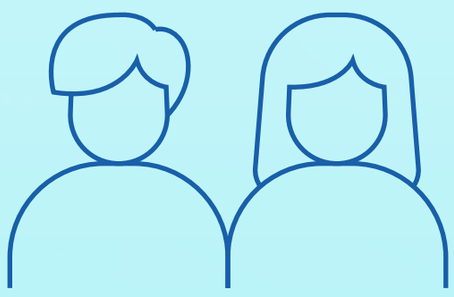
FALSE

Congenital, childhood-onset and adult-onset phenotypes of DM1 have cognitive involvement across multiple domains[1]

Congenital DM1:
cognitive impairment typically presents as neurodevelopmental and intellectual issues, and is not progressive[2,3]



Childhood-onset DM1:
learning difficulties rather than skeletal muscle impairment are the most frequent initial symptoms[1]



Adult-onset DM1:
cognitive decline is progressive, resembling accelerated aging[4–6]

NEXT

DM1, myotonic dystrophy type 1.

References: 1. Rahm L, et al. *Nature Rev Neurol.* 2025;21(11):623–641; 2. Modoni A, et al. *JAMA Neurol.* 2004;61(12):1943–1947; 3. Lindeblad G, et al. *Dev Med Child Neurol.* 2019;61(10)1214–1220; 4. Winblad S, et al. *Eur J Neurol.* 2016;23(9):1471–1476; 5. Gallais B, et al. *Neuromuscular Disord.* 2017;27(1):61–72; 6. Meinke P, et al. *Front Neurol.* 2018;9:601.

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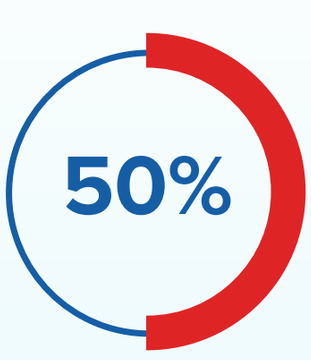
COGNITION



>50% of people living with DM1 experience cognitive impairments[1]

Impact on individuals living with DM1

Cognitive impairments include deficits in executive function, attention, working memory, psychomotor function, and visual memory, among others[1,2]

Tap the buttons to learn more

Executive function: Reduced initiative and inactivity are prominently and consistently found in individuals with DM1[2]

Working memory: Deficits in working memory and short-term memory are prevalent, causing difficulties with learning and recalling recent events[1,3]

Attention: Attentional deficit hyperactive disorder is frequent, often diagnosed in young children with DM1[2]

Cognitive function is associated with QoL – poorer cognitive ability in attention/working memory and processing speed have been shown to be associated with lower QoL[1]

DM1, myotonic dystrophy type 1; **QoL,** quality of life.

References: 1. Fujino H, et al. *Muscle Nerve.* 2018;57(5):742–748; 2. Meola G & Sansone *V. Muscle Nerve.* 2007;36: 294–306; 3. Wu Y, et al. *Front Cell Neurosci.* 2024;18:1369332.

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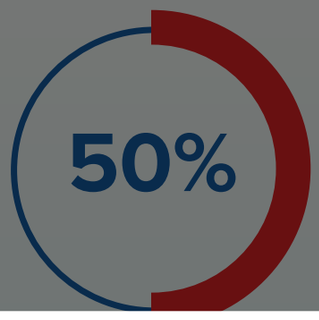
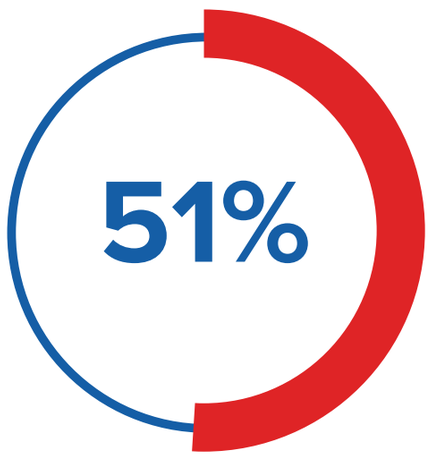
COGNITION

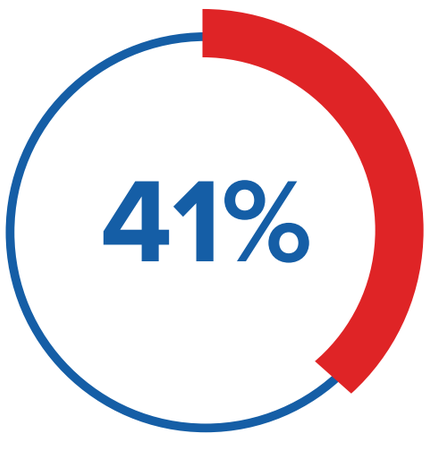


>50% of people living with DM1 experience cognitive impairments[1]

Executive function



Have difficulty putting thoughts into words[1]



Have difficulty planning daily activities[1]

“I look at a diagram now, and it is like reading a foreign language… I just can’t process the information.”

Adult with adult-onset DM1[2]

DM1, myotonic dystrophy type 1.

Quote from individual with DM1 taken from White M. *Ther Innov Regul Sci.* 2020;54(5):1010–1017, and licensed under a CC-BY 4.0 Creative Commons license.

References: 1. Hagerman KA, et al. *Muscle Nerve.* 2019;59:457–464; 2. White M. *Ther Innov Regul Sci.* 2020;54(5):1010–1017.

SELECT TOPIC

CNS, central nervous system; **DM1,** myotonic dystrophy type 1; **QoL,** quality of life.

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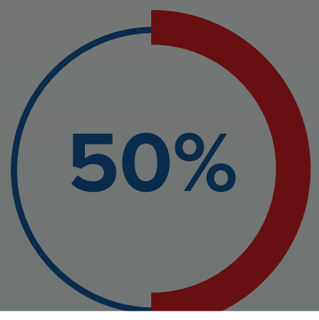
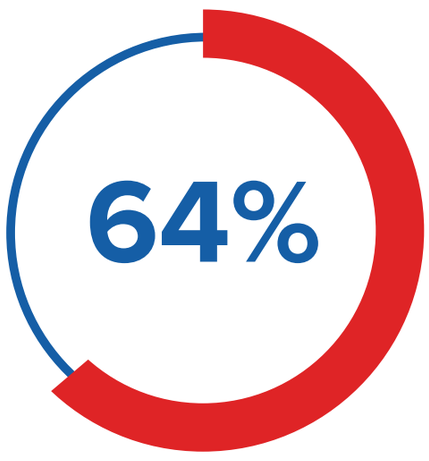
COGNITION



>50% of people living with DM1 experience cognitive impairments[1]

Working memory



Have difficulty remembering things[1]

"If you speak too long, I will forget what you said in the beginning. I probably will interrupt you because I have forgotten what you had been saying... When I read, by the time I get to the end of the page, I have forgotten what I read."

Adult with juvenile-onset DM1[2]

"When watching a movie, I usually end up rewinding scenes over and over and over again to fully grasp the storyline."

Adult with juvenile-onset DM1[2]

DM1, myotonic dystrophy type 1.

Quotes from individuals with DM1 taken from White M. *Ther Innov Regul Sci.* 2020;54(5):1010–1017, and licensed under a CC-BY 4.0 Creative Commons license.

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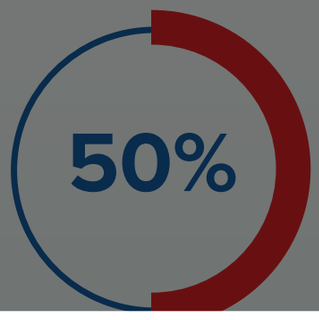
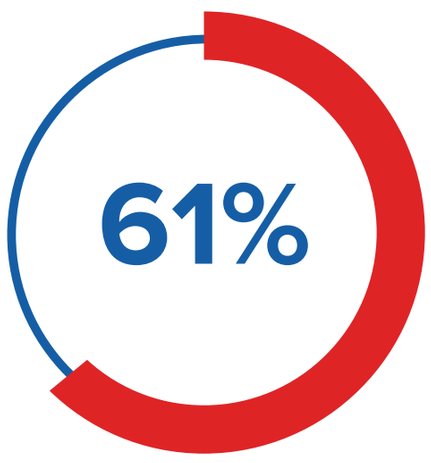
COGNITION

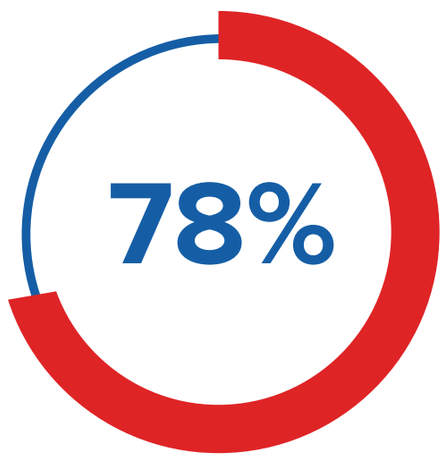


>50% of people living with DM1 experience cognitive impairments[1]

Attention



Have difficulty concentrating[1]



Have difficulty with alertness or difficulty staying awake[1]

"I'm not able to drive, partly due to my attention deficit disorder."

Adult with juvenile-onset DM1[2]

"My attention span is very short. I think this has gotten worse since I was a teenager. I get distracted very easily, and then I don't know what I was doing... I lose interest before I finish almost anything."

Adult with juvenile-onset DM1[2]

DM1, myotonic dystrophy type 1.

Quotes from individuals with DM1 taken from White M. *Ther Innov Regul Sci.* 2020;54(5):1010–1017, and licensed under a CC-BY 4.0 Creative Commons license.

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PERSONALITY AND EMOTION

TRUE OR FALSE?

DM1 muscle involvement is the only factor that impairs social participation and satisfaction in individuals with DM1

TRUE

FALSE

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PERSONALITY AND EMOTION

FALSE

CNS involvement in DM1 frequently leads to emotional and/or personality symptoms that can impair social satisfaction and participation[1]

NEXT

CNS, central nervous system; **DM1,** myotonic dystrophy type 1.

Reference: 1. Meola G, Sansone V. *Muscle Nerve.* 2007;36(3):294–306.

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Understanding how
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PERSONALITY AND EMOTION

CNS involvement in DM1 impacts various measures of behavior/personality patterns and emotion

Signs and symptoms of behavioral and emotional impact in DM1[1–4]

Behavior/personality patterns[1,4]

Apathy

Avoidance

Obsessive compulsive

Passive aggressive

Dependent

Facial emotion recognition deficit

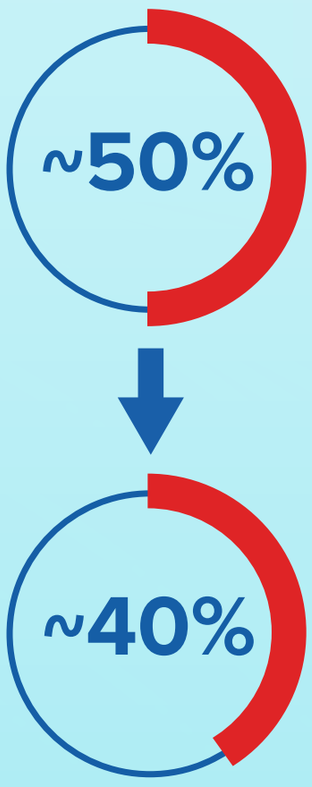
Emotion[1–3]

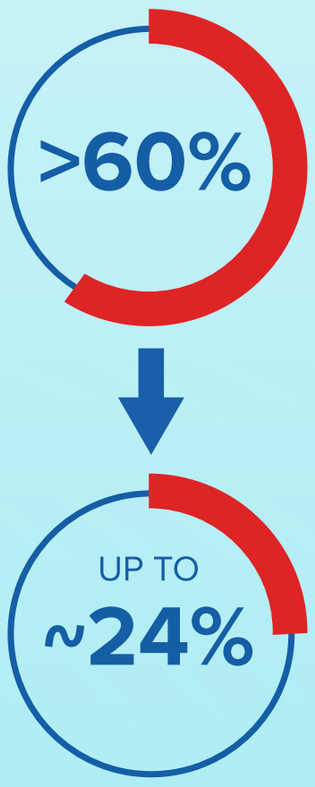
Depression

Decreased emotional participation

Emotional burden

~50% experience behavioral/personality issues[2]





>60% experience emotional issues[2]

~40% experience apathy[5]

Up to ~24% experience depression[3]

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CNS, central nervous system; **DM1,** myotonic dystrophy type 1.

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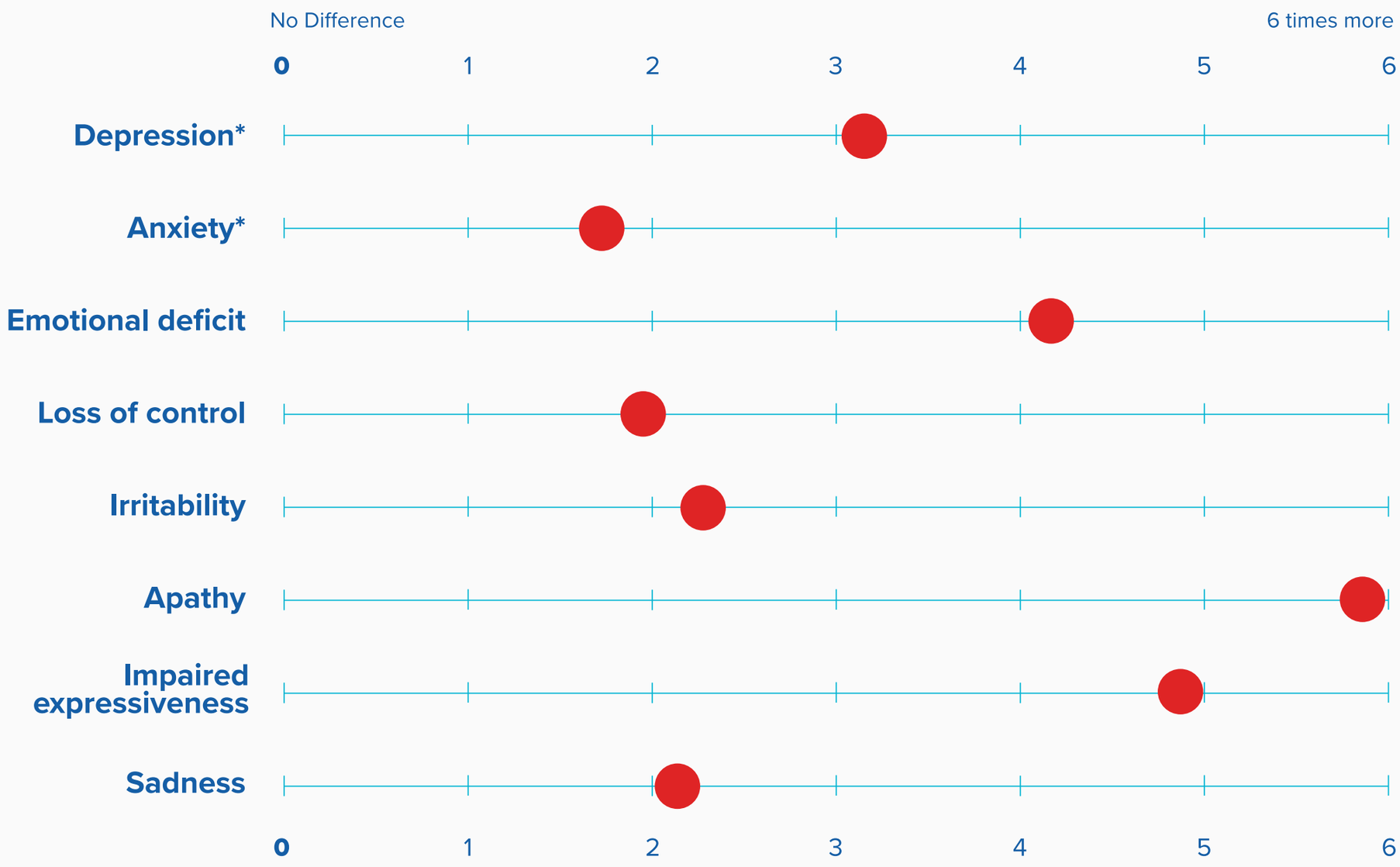
PERSONALITY AND EMOTION

Impact on individuals living with DM1

DM1 in adults is often associated with impaired psychological wellbeing, including feelings of anxiety, depression, frustration, and low self-esteem, placing a substantial burden on those living with the condition[1]

Psychological evaluations for people with myotonic dystrophy compared with a control population[2]



*Depression measured by MADRS scale, anxiety by Tyrer scale, other outcomes by EHD

Symptoms such as higher apathy and depression scores correlate with lower QoL[3]

NEXT

DM1, myotonic dystrophy 1; **EHD,** Echelle d'Humeur (translation: Depressive Mood Scale); **MADRS,** Montgomery-Åsberg Depression Rating Scale; **QoL,** quality of life.

References: 1. Landfeldt E, et al. *J Neurol.* 2019;266(4):998–1006;
2. Bungener C, et al. *J Neurol Neurosurg Psychiatry.* 1998;65:353–356; 3. Fujino H, et al. *Muscle Nerve.* 2018;57(5):742–748.

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PERSONALITY AND EMOTION

Apathy in DM1 may be centrally driven, given its association with overall cognitive status but lack of association with factors such as age, motor disability, and fatigue[1]

Apathy impacts many different aspects of daily living, including social participation and productivity[1]

Depression in DM1 is not only secondary to living with chronic illness[2]

Rates of depression in DM1 are higher than in the general population and in comparison to other somatic diseases[3]

Impact on caregivers

Caregivers report a greater care burden when the individuals they care for have higher levels of depressive symptoms[4]

NEXT

DM1, myotonic dystrophy type 1.

References: 1. Gallais B, et al. *BMC Neurol.* 2015;15:148; 2. Schneider-Gold C, et al. *PLoS One.* 2015;10(6):e0130352; 3. Minier L, et al. *J Neuromuscul Dis.* 2018;5(3):279–294; 4. Kurauchi G, et al. *J Neuromuscul Dis.* 2019;6(4):527–536.

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Date of preparation: July 2026. MED-01247.

Understanding how
DM1 affects the brain

PERSONALITY AND EMOTION

Causes

CNS changes play a key role in behavioral and emotional changes, such as apathy and depression

A study of 39 individuals with adult-onset DM1 showed greater white matter abnormality was associated with higher apathy scores[1]

A study of 12 individuals with juvenile or classical DM1 showed a trend towards white matter brainstem atrophy and depression grade[2]

SELECT TOPIC

CNS, central nervous system; **DM1,** myotonic dystrophy type 1.

References: 1. Miller JN, et al. *Front Neurol.* 2021;12:700796. 2. Schneider-Gold C, et al. *PLoS One.* 2015; 10(6):e0130352.

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Understanding how
DM1 affects the brain

FATIGUE AND EDS

TRUE OR FALSE?

Muscle weakness and obstructive sleep apnea are the causes of fatigue and EDS in DM1

TRUE

FALSE

DM1, myotonic dystrophy type 1; **EDS,** excessive daytime sleepiness.

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Understanding how
DM1 affects the brain

FATIGUE AND EDS

FALSE

Although both muscle weakness and obstructive sleep apnea can contribute to fatigue and EDS, morbidity is primarily due to the CNS-driven impact of DM1[1,2]

Sleep architecture is altered in individuals with DM1, and associated with structural brain changes, which suggests that sleep–wake dysregulation in DM1 is likely primarily due to CNS-driven pathology[3,4]

NEXT

CNS, central nervous system; **DM1,** myotonic dystrophy type 1; **EDS,** excessive daytime sleepiness.

References: 1. Angelini C, et al. *Neuromuscul Disord.* 2012;22 Suppl 3(3-3):S214–S220;
2. Dauvilliers Y, et al. *Sleep Med Rev.* 2012;16(6):539–545; 3. Laberge L, et al. *Sleep Med.* 2026;108781;
4. Hamilton MJ, et al. *Neuromuscul Disord.* 2022;32(5):377–389.

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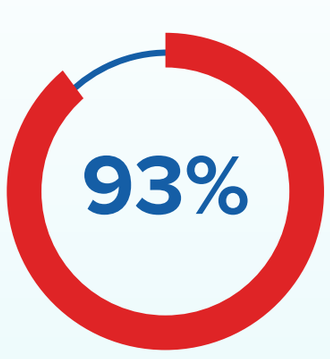
Understanding how
DM1 affects the brain

FATIGUE AND EDS



Have fatigue and EDS

EDS and fatigue are among the most common and debilitating complaints in DM1, affecting a majority of individuals living with DM1[1,2]

Impact on individuals living with DM1

Fatigue and EDS have profound effects on the daily life of individuals living with DM1[2]

The following quotes were given by individuals living with DM1 and their carers at a large meeting of 350 members of the myotonic dystrophy community in 2017[2]

"I deal with extreme fatigue and daytime sleepiness... I would sometimes fall asleep in class."

Young adult with juvenile-onset DM1

"At night I have trouble falling asleep and staying asleep."

Adult with adult-onset DM1

"I'm so tired I just can't do anything... It's almost like you feel sick, your eyes are really heavy... I can't even move my body."

Adult with DM1

"It takes me about an hour to fully wake up and function... I'm easily agitated and frustrated in the morning."

Adult with juvenile-onset DM1

"My son says the worst daily thing is the extreme sleepiness he feels driving home after college or work."

Mother of adult son living with juvenile-onset DM1

"I have dreams where you think you are awake and doing things. You don't know what's real."

Young adult with juvenile-onset DM1

NEXT

DM1, myotonic dystrophy type 1; **EDS,** excessive daytime sleepiness.

Quotes from individuals with DM1 taken from White M. *Ther Innov Regul Sci.* 2020;54(5):1010–1017, and licensed under a CC-BY 4.0 Creative Commons license.

References: 1. Hagerman KA, et al. *Muscle Nerve.* 2019;59(4):457–464; 2. White M. *Ther Innov Regul Sci.* 2020;54(5):1010–1017.

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Understanding how
DM1 affects the brain

FATIGUE AND EDS

Causes

EDS and fatigue both have central (CNS-driven) and peripheral (muscle-driven) causes[1,2]

Causes of EDS in DM1[1]

Muscle-driven EDS

Obstructive sleep apnea due to craniofacial changes and sleep disordered breathing arising from respiratory muscle impairment

CNS-driven EDS

Alterations in sleep structure (phases of sleep) due to changes in brain structure and sleep disordered breathing due to impaired central respiratory drive

Causes of fatigue in DM1[2]

Muscle-driven fatigue

Peripheral fatigue due to atrophy of muscle fibers

CNS-driven fatigue

Central fatigue due to cortical atrophy and white matter lesions that reduces voluntary muscle activation during exercise

Sleep dysregulation in DM1[3–5]

Actigraphy shows poorer sleep quality and delayed sleep–wake episodes compared with healthy controls.[3] Individuals with DM1 show increased proportions of slow-wave and REM sleep, and dysregulation of REM sleep.[4,5] Circadian rhythm sleep disorders may be more common in DM1[3]

NEXT

CNS, central nervous system; **DM1,** myotonic dystrophy type 1; **EDS,** excessive daytime sleepiness; **REM,** rapid eye movement.

References: 1. Hoxhaj D, et al. *Front Neurol.* 2024;15:1389949;
2. Angelini C, et al. *Neuromuscul Disord.* 2012;22 Suppl 3(3-3):S214–S220; 3. Laberge L, et al. *Sleep Med.* 2026;108781;
4. Hamilton MJ, et al. *Neuromuscul Disord.* 2022;32(5):377–389; 5. Romigi A, et al. *Curr Neurol Neurosci Rep.* 2018;18:102.

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Understanding how
DM1 affects the brain

FATIGUE AND EDS

What do we know about the role of the CNS in causing sleep dysregulation, EDS, and fatigue in DM1?

Tap the boxes to learn more

EDS in DM1 is not always accompanied by sleep apnea, and non-invasive ventilation (e.g. CPAP) is not always effective[1,2]

Individuals living with DM1 have shown a “narcolepsy-like” phenotype[3]

Measures of sleep architecture and EDS have been shown to correlate with changes in brain structure in individuals living with DM1[4]

Worsening fatigue can be independent of muscle weakness progression[5]

Sleep-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[6]

SELECT TOPIC

CNS, central nervous system; **CPAP,** continuous positive airway pressure; **DM1,** myotonic dystrophy type 1; **EDS,** excessive daytime sleepiness.

References: 1. Ferrari Aggradi CR, et al. *Can Respir J.* 2022:2321909; 2. West SD, et al. *J Neuromuscul Dis.* 2016;3(4):529–537; 3. Romigi A, et al. *Curr Neurol Neurosci Rep.* 2018;18:102; 4. Hamilton MJ, et al. *Neuromuscul Disord.* 2022;32(5):377–389; 5. Peric S, et al. *Acta Myol.* 2019;38(4):239–244; 6. Subramony SH, et al. *Muscle Nerve.* 2020;62:309–320.

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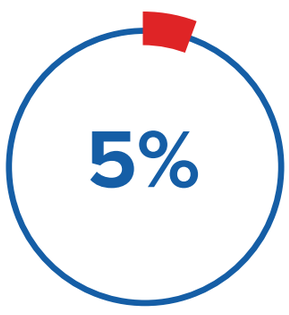
Understanding how
DM1 affects the brain

EDS in DM1 is not always accompanied by sleep apnea, and non-invasive ventilation (e.g. CPAP) is not always effective[1,2]

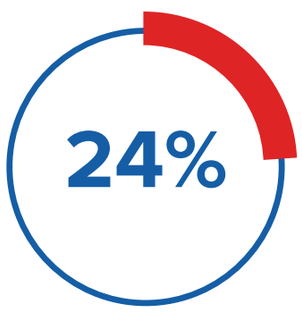
Although a proportion of individuals with DM1 present with OSA, which can arise due to craniofacial changes, sleep disordered breathing driven by the CNS, such as central sleep apnea and central hypoventilation, is also observed[1,3]

Non-invasive ventilation such as CPAP has shown limited efficacy in DM1, which further supports the role of the CNS in sleep disordered breathing[2,4]

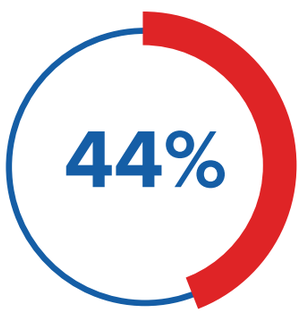
In a single-center cohort of 151 individuals with adult-onset DM1[1]



Had OSA

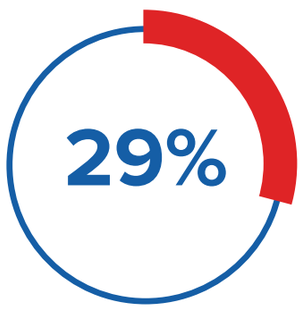


Had EDS (comprising 16/66 evaluable individuals living with DM1)



Had respiratory parameters that would require NIV

In a prospective cohort study of 120 individuals with DM1 who were referred for sleep and ventilation assessment[2]



Benefitted from targeted sleep therapy (CPAP, NIV and modafinil)

Sleep and ventilation problems remain unresolved in ~70% of individuals who receive targeted sleep therapies[2]

CNS, central nervous system; **CPAP,** continuous positive airway pressure; **DM1,** myotonic dystrophy type 1; **EDS,** excessive daytime sleepiness; **NIV,** non-invasive ventilation; **OSA,** obstructive sleep apnea.

References: 1. Ferrari Aggradi CR, et al. *Can Respir J.* 2022:2321909; 2. West SD, et al. *J Neuromuscul Dis.* 2016;3(4):529–537; 3. Hoxhaj D, et al. *Front Neurol.* 2024;15:1389949; 4. Patil SP, et al., *J Clin Sleep Med* 2019;15:2:335–343.

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Understanding how
DM1 affects the brain

FATIGUE AND EDS

What do we know about the role of the CNS in causing sleep dysregulation, EDS, and fatigue in DM1?

Tap the boxes to learn more

Individuals living with DM1 have shown a “narcolepsy-like” phenotype[1]

Multiple sleep studies have reported the presence of a “narcolepsy-like” phenotype in individuals with DM1[1]

In healthy individuals, REM sleep usually occurs 60–90 minutes after falling asleep, and mostly in the second half of the night[2]

However, individuals with DM1 can show SOREMP, which occurs shortly after falling asleep, and is one of the hallmarks of narcolepsy[1,3]

Narcolepsy is driven by reductions in the neuropeptide orexin, and some studies have also reported reduced orexin levels in the CSF of individuals with DM1, although these findings are not consistent across all studies[1,4]

CSF, cerebrospinal fluid; **DM1,** myotonic dystrophy type 1; **REM,** rapid eye movement; **SOREMP,** sleep-onset REM period.

References: 1. Romigi A, et al. *Curr Neurol Neurosci Rep.* 2018;18:102; 2. Feriante J, Araujo JF. Physiology, REM Sleep. [Updated 2023 Feb 13]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK531454/; 3. Slowik JM, Collen JF, Yow AG. Narcolepsy. [Updated 2023 Jun 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459236/; 4. Mahoney CE, et al. *Nat Rev Neurosci* 2019;20(2):83–93.

SELECT TOPIC

CNS, central nervous system; **CPAP,** continuous positive airway pressure; **DM1,** myotonic dystrophy type 1; **EDS,** excessive daytime sleepiness.

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Understanding how
DM1 affects the brain

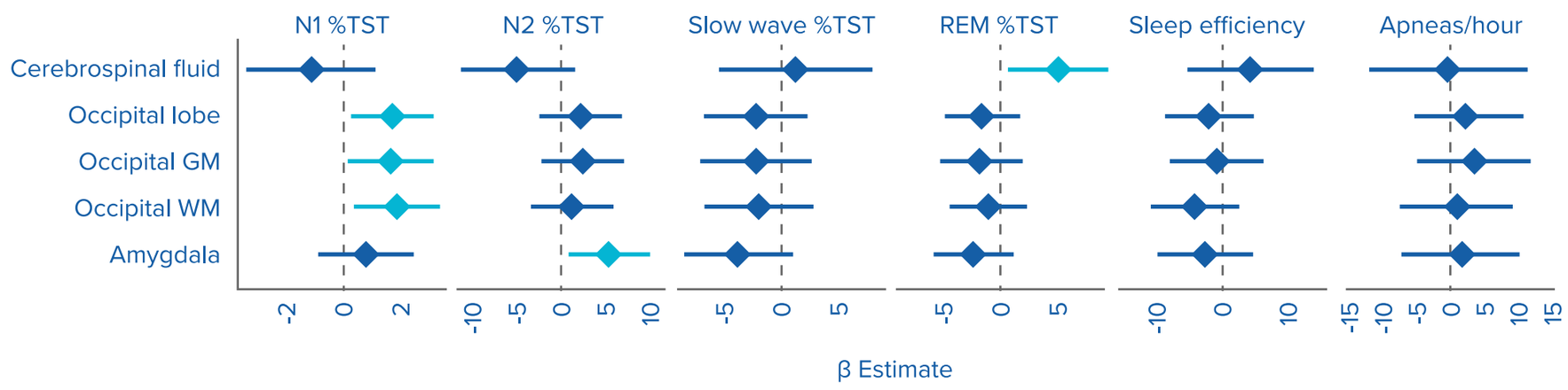
FATIGUE AND EDS

What do we know about the role of the CNS in causing sleep dysregulation, EDS, and fatigue in DM1?

Measures of sleep architecture and EDS have been shown to correlate with changes in brain structure in individuals living with DM1[1]

Measures of sleep architecture and EDS have been shown to correlate with changes in brain volume in individuals with DM1, suggesting that changes in sleep are linked to a disease process in the CNS[1]

Statistically significant relationships (light blue bars; $p<0.05$) between sleep measures and regional brain volumes in a study of 36 participants with DM1[1]



Reduced density of serotonergic neurons – considered to be involved in sleep regulation – has been observed in the individuals with myotonic dystrophy, supporting a direct CNS impact on sleep[2]

Note: N1 – light sleep; **N2 –** deeper sleep[3]

CNS, central nervous system; **DM1,** myotonic dystrophy type 1; **EDS,** excessive daytime sleepiness; **GM,** grey matter; **MD,** myotonic dystrophy; **N1,** stage 1 sleep; **N2** stage 2 sleep; **REM,** rapid eye movement; **TST,** total sleep time; **WM,** white matter.

Figure reference: Hamilton MJ, et al. *Neuromuscul Disord.* 2022;32(5):377–389. Licensed under a CC-BY 4.0 Creative Commons license.

References: 1. Hamilton MJ, et al. *Neuromuscul Disord.* 2022;32(5):377–389; 2. Ono S, et al. *Neurology.* 1998;50(2):535–538; 3. Patel AK, et al. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK526132/.

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Understanding how
DM1 affects the brain

FATIGUE AND EDS

What do we know about the role of the CNS in causing sleep dysregulation, EDS, and fatigue in DM1?

Tap the boxes to learn more

Worsening fatigue can be independent of muscle weakness progression[1]

Fatigue in DM1 has been to have both central (CNS) and peripheral (muscle) components[2]

In a 7-year longitudinal study of 64 individuals with DM1, three assessments were used investigate patterns of fatigue, muscle weakness and EDS[1]

Fatigue	Muscle weakness	EDS
FSS	MIRS	DSS

In this study, change in fatigue was not correlated with change in muscle weakness. Moderate correlation was found between the change in fatigue and EDS ($p<0.05$)[1]

CNS, central nervous system; **DM1,** myotonic dystrophy type 1; **EDS,** excessive daytime sleepiness; **FSS,** Krupp's Fatigue Severity Scale (FSS); **MIRS,** Muscular Impairment Rating Scale; **DSS,** Daytime Sleepiness Scale.

References: 1. Peric S, et al. *Acta Myol.* 2019;38(4):239–244;
2. Angelini C, Tasca E. et al. *Neuromuscul Disord.* 2012;22 Suppl 3(3-3):S214–S220.

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