CENTRAL NERVOUS SYSTEM (CNS) INVOLVEMENT IN MYOTONIC DYSTROPHY TYPE 1 (DM1)

Dyne Medical Central

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 elucidated[5–7]

- 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]

Percentage of individuals with DM1 experiencing symptoms[10,11]

- 50% — **Cognitive impact**[9,10] e.g. executive function, attention, working memory
- ~50% — **Behavior and personality patterns**[9,12] e.g. apathy, avoidance, facial emotion recognition deficit
- >60% — **Emotional impact**[9,13] e.g. emotional burden, depression, emotional participation
- 93% — **Fatigue**[14] e.g. psychosocial functioning, social isolation
- 93% — **Excessive daytime sleepiness**[9,15] e.g. social functioning, employment, QoL

CNS changes leading to dysregulated sleep[16,17,a]

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: [a]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.
Abbreviations: CNS, central nervous system; **DM1,** myotonic dystrophy type 1; **QoL,** quality of life.

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