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SLEEP, SLEEP DISORDERED BREATHING, AND NOCTURNAL HYPOVENTILATION IN CHILDREN WITH NEUROMUSCULAR DISEASES

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I. SUMMARY

Sleep disordered breathing (SDB) is now well recognized in children with neuromuscular diseases (NMD) and may lead to significant morbidity and increased mortality. Predisposing factors to SDB in children with NMD include reduced ventilatory responses, reduced activity of respiratory muscles during sleep and poor lung mechanics due to the underlying neuro-muscular disorder. SDB may present long before signs of respiratory failure emerge. When untreated, SDB may contribute to significant cardiovascular morbidities, neuro-cognitive deficits and premature death. One of the problems in detecting SDB in patients with NMD is the lack of correlation between lung function testing and daytime gas exchange. Polysomnography is the preferred method to evaluate for SDB in children with NMD. When the diagnosis of SDB is confirmed, treatment by non-invasive ventilation (NIV) is usually recommended. However, other modalities of mechanical ventilation do exist and may be indicated in combination with or without other supportive measures.

Keywords

Hypoventilation; Neuromuscular diseases (NMD); Non invasive ventilation (NIV); Obstructive sleep apnoea (OSA); Polysomnography; Sleep disordered breathing (SDB)

II. INTRODUCTION

Sleep disordered breathing (SDB) refers to a group of respiratory disorders that occur in sleep or are exacerbated during sleep. These include: central apnoea, hypoventilation, and the spectrum of obstructive sleep apnoea (OSA). SDB may disrupt normal ventilation and sleep architecture (1). In addition, SDB is associated with significant cardiovascular morbidities and neurocognitive deficits (2). The presence of SDB in children has been reported in a wide range of NMD including: spinal muscular atrophy (3–5), myotonic dystrophy (6), Duchenne muscular dystrophy (7–9), cerebral palsy (10), peripheral neuropathies (11), congenital myopathies (5,12), metabolic myopathies (5) and myasthenia gravis (12). Moreover, SDB has been shown to be amplified in patients with NMD, affecting their quality of life and longevity (9,13).

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The prevalence of SDB in children with NMD is not well studied. No large cross-sectional or longitudinal studies that could determine the precise prevalence, incidence and range of SDB with specific NMD exist. Nevertheless, it seems that the prevalence is much higher than the 2% reported in the general population (14). It is estimated that 27–62% (7,15) of children and 36–53% of adults (8,12,16) with NMD have SDB. The wide range in these reports may be explained by differences in the populations that were studied in regard to age and type of NMD, different methodologies of testing and different definitions of respiratory abnormalities.

III. PATHOPHYSIOLOGY OF SLEEP DISORDERS IN NEUROMUSCULAR DISEASE

NMD are a heterogeneous group of disorders and patients may present with varying degrees of respiratory muscle weakness affecting ventilation. A full array of sleep related breathing abnormalities have been reported including: airflow limitation, hypoventilation, upper airway obstruction, and central apnoea. However, the type and severity of SDB is most influenced by the primary disorder, age of the patient, and the type and extent of the muscles involved (Table 1).

Ventilatory Responses

To understand the pathophysiology of SDB in children with NMD, it is useful to review the effects of sleep on breathing in normal individuals and how these may affect children with respiratory muscle weakness, particularly during REM sleep. The ventilatory response plays an important role in regulating breathing in sleep and includes several components. The first are the sensors, including central and peripheral chemoreceptors and mechanoreceptors. The chemoreceptors relay minute changes in PaO_2 , PaCO_2 , and pH through afferent neurons to a central controller within the brain stem where the information is integrated. From there, afferent neurons relay their output to the effectors (upper airway dilators, intercostals, diaphragm, etc.), that produce the response. In such a way, the feedback mechanism can tightly regulate any change in the blood gas by changing minute ventilation.

Sleep in healthy individuals is associated with a reduction in the slope of the ventilatory responses to both hypercapnia and hypoxia compared to wakefulness (17,18). This phenomenon is responsible for the reduction in minute ventilation by 1–2 litres per minute [LPM] and the increase in the PaCO_2 by 2–8 mmHg and decrease in PaO_2 by 2–8 mmHg, observed in sleep. The drop in minute ventilation progresses through sleep stages reaching its maximal attenuation in the phasic stage of REM sleep (19).

Traditional tests of the ventilatory chemoreceptor response assess the minute ventilation response to applied hypercapnia and hypoxia. These tests can be problematic in NMD patients due to muscular weakness, fatigue, and inability to tolerate prolonged hypercapnia or hypoxia.

To overcome these limitations, a technique that does not require prolonged respiratory muscle effort can be used. This method, known as the mouth occlusion test ($\text{P}_{0.1}$) measures the pressure at the mouth 100 ms after inspiratory occlusion under various degrees of hypercapnic or hypoxic conditions. Except for some subjects with Arnold-Chiari malformation type 2, noted to have low central and peripheral chemoreceptor sensitivity (20), and some subjects with myotonic dystrophy found to have a central controller defect (21), children with NMD were found to have a normal ventilatory drive and are not considered to have either a chemoreceptor or a central controller abnormality during wakefulness or sleep (22).

Respiratory Muscles

The most important impact of sleep on patients with NMD is the effect on respiratory muscle function. In healthy subjects, sleep onset is associated with the reduction in tonic activity of the upper airway dilator muscles, particularly the genioglossus. This reduction progresses to a maximum in REM sleep and can increase upper airway resistance leading to SDB in susceptible patients (23). Similar tonic reduction occurs to intercostal muscles leading to a reduction in functional residual capacity (FRC) and oxygen reserves. The diaphragm on the other hand, maintains normal activity in NREM sleep but gradually loses tonic activity in REM sleep with the appearance of clustered pauses that contributes to further reduction in FRC in this phase. Thus, healthy subjects are susceptible to respiratory disturbances and gas exchange abnormalities particularly in REM sleep when upper airway resistance is increased and FRC is decreased. This susceptibility is amplified in NMD patients due to pre existing respiratory muscles weakness and could explain the high prevalence of SDB in these patients.

A primary upper respiratory muscle involvement may be present in children with cerebral palsy, poliomyelitis, myotonic dystrophy, myelomeningocele, hereditary sensory and motor neuropathies (Charcot-Marie-Tooth), and certain congenital myopathies, particularly due to bulbar involvement. Intercostal muscle involvement is common in most NMD with generalized muscle weakness, and diaphragm involvement is present in spinal muscular atrophy, poliomyelitis, high cervical cord injury, and certain mitochondrial, metabolic and congenital myopathies as well as in Duchenne and Becker muscular dystrophies.

Children with NMD may also be subject to common known risks for SDB in children, adenotonsillar hypertrophy and obesity. In such children, SDB may be more severe in comparison to otherwise healthy individuals with adenotonsillar hypertrophy and or obesity alone.

As mentioned above, the type and severity of SDB is most influenced by the primary disorder and the type and extent of the muscles involved. For example, in patients with only upper airway and intercostal muscles weakness but intact diaphragm function, the increased negative intrathoracic pressure induced by the diaphragm during inspiration will lead to upper airway narrowing and airway obstruction due to inability of the upper airway musculature to dilate the airway. The above condition would be typical of a patient with Duchenne muscular dystrophy in early stages of the diseases (Figure 1). However, with progression of the disease and with diaphragm involvement, a lower negative intra thoracic pressure will be generated that will not be sufficient to fully collapse the upper airway. Thus, the predominant respiratory event will be obstructive hypopnoea and hypoventilation (Figures 2 and 3).

Lung mechanics change during sleep and result in respiratory deficiencies in patients with NMD particularly due to an increase in chest wall compliance and changes in diaphragm position and strength (24). In order to maintain adequate ventilation, patients compensate by recruiting not only accessory inspiratory muscles but also abdominal muscles. Contraction of abdominal muscles produces expiration below FRC allowing passive inspiration with recoil of the chest wall. Such changes in muscle activity increase work of breathing. Thus, to improve energy expenditure and maintain adequate minute ventilation simultaneous changes in respiratory patterns are noted and include a rise in respiratory rate with reciprocal drop in tidal volume.

In addition, patients with NMD are found to have low muscle endurance and are constantly at risk of developing respiratory muscle fatigue resulting in SDB (25). In this regard, the tension-time index of the respiratory muscles (TTmus) has been suggested as a sensitive test to assess how close a subject is to respiratory fatigue/failure. (26). Attempts to improve muscle

endurance by day time respiratory muscle training has been studied with various results. However, it is unknown if such techniques are useful to improve SDB

Finally, a poor and ineffective cough is found in all patients with respiratory muscle weakness. This can be demonstrated by reduced maximal inspiratory and expiratory static pressures (MIP and MEP, respectively). These patients are at increased risk of developing mucus plugging and ventilation perfusion inequalities from airway secretions, particularly during sleep when the cough reflex is suppressed due to a higher arousal threshold.

Arousal Threshold

In normal subjects, progression to deeper sleep stages is associated with a higher arousal threshold and reduced arousal response to various stimuli such as: hypercarbia, hypoxemia, and resistive loading. This poor response in conjunction with normal reduction in chemosensitivity noted in sleep can increase the risk for SDB in subjects with altered upper airway function or generalized respiratory muscle weakness.

Scoliosis

The most frequently encountered musculoskeletal complication in NMD children is scoliosis. Scoliosis contributes to reduced chest wall and lung compliance and increases the risk for SDB by mechanisms of hypoventilation, atelectasis and ventilation perfusion mismatch, and increased work of breathing and fatigue. In most cases repair of scoliosis by stabilization of the spine reduces morbidity by preventing worsening of scoliosis and preserving chest and lung mechanics (27).

Obesity

Obesity is a known risk factor for SDB in children today and exacerbates many of the basic causes of SDB (14). Children with specific NMD such as Duchenne muscular dystrophy and myotonic dystrophy may have an increased metabolic risk for cardiovascular disease including: high BMI, low levels of high-density lipoprotein cholesterol, and high triglyceride, due to decreased motor activity and exercise (16,28).

Altered Brain Structure or Function

Several NMD including hypoxic ischemic encephalopathy, Arnold-Chiari malformation type 2, mitochondrial myopathy, and myotonic dystrophy are associated with alterations in either brain structure or function. These conditions may lead to significant SDB ranging from central apnoea and periodic breathing to the spectrum of OSA.

IV. SLEEP DISORDERED BREATHING IN SPECIFIC NEUROMUSCULAR DISEASES ACCORDING TO LEVEL OF DEFECT

Upper Motor Neuron

Childhood disorders affecting upper motor neuron and that increase the risk for SDB include: perinatal hypoxic encephalopathy, cerebral palsy, and traumatic brain injury. The neuromuscular manifestations of these disorders may include: poor upper airway muscle control, spasticity/hypotonia, seizures, poor nutritional status, gastro-oesophageal reflux, impairment of airway clearance, scoliosis and poor pulmonary reserve.

Children with hypoxic brain injuries may have severe forms of SDB requiring additional surgical procedures after adenotonsillectomy such as repeated adenoidectomy and, less commonly, uvulopalatopharyngoplasty [UPPP]. A decade ago, tracheostomy was estimated to be required in about 15% of children with severe SDB (10). In addition to the surgical

intervention, non-invasive ventilation is often required. It is usually well tolerated and has been shown to improve quality of life in these children (13).

Brain Stem

Myelomeningocele and Arnold-Chiari malformation type 2—Myelomeningocele (MMC) is a neurodysplasia of incomplete closure of the spinal canal that presents from birth. It could appear anywhere along the spinal cord but most commonly in the thoracic, lumbar, lumbosacral, or sacral regions. At times, MMC is associated with Arnold-Chiari malformation (ACM) type 2 that is the downward displacement of the medulla and cerebellar tonsils with extension of the fourth ventricle into the spinal canal. The latter condition is commonly associated with hydrocephalus and SDB.

In a study on 83 children, Waters et al. (29) noted moderate-severe SDB in 20% of children with MMC and ACM type 2. Of these 2/3 had central apnoeas and 1/3 had an obstructive pattern of SDB. They have suggested that the pathogenesis of SDB in these children involves the functional level of the spinal lesions, congenital and acquired brainstem abnormalities, pulmonary function abnormalities, as well as disorders of upper airway control and arousal (30,31)

Spinal Cord Injury

Pediatric spinal cord injuries usually result from an abrupt flexion, extension, rotation, or distraction of the cord and lead to various clinical outcomes depending on the level and extent of injury. Injuries above C4 are most severe and require chronic mechanical ventilation due to involvement of all respiratory muscles. Injuries between C4 and T6 may require only partial ventilatory assistance since the function of the diaphragm may be preserved (32,33).

Birth trauma is the leading cause of injury in the first year of life, typically affecting the upper cervical spine. Other traumatic causes include: falls, pedestrian-automobile accidents, motor vehicle accidents and sports related injuries. Non traumatic causes include: rheumatoid arthritis, infections and tumours of the spine. Finally, children with Down's syndrome, ACM, and achondroplasia may be at risk to develop spinal cord injuries due to instability of the cervical spine or cord compression.

Motor Neuron

Spinal muscular atrophy—Spinal muscular atrophy (SMA) is a disorder affecting the motor neurons of the spinal cord and brainstem. Type I is known as infantile SMA or Werdnig Hoffmann syndrome. It is most severe and manifests in the first year of life with hypotonia and rapidly progressive respiratory insufficiency. In type II or intermediate SMA, respiratory muscle weakness is usually recognized between 6 and 18 months. It progresses slowly and gradually over the life span. Type III known as Kugelberg-Welander syndrome affects older children in adolescent years and is a mild disorder.

Sleep disordered breathing is common in all forms and needs to be evaluated in all children. Mellies et al. (4) studied 12 children (7.8 ± 1.9 years) by polysomnography, and found 7 (six with type I and one with type II) to have SDB and alterations in sleep architecture. Non-invasive ventilation during sleep completely eliminated SDB and normalized sleep architecture in these children. Similar findings were reported by Petrone et al. (34) in 9 children between 2–33 months of age and who were studied before and after initiation of non-invasive ventilation using bilevel positive airway pressure ventilation. Significant improvement in all respiratory parameters including apnoea hypopnoea index (AHI), oxygen desaturation, PtcPCO₂, and respiratory mechanics measured by phase angle were noted.

Peripheral Nerve

Charcot-Marie-Tooth—Hereditary motor and sensory neuropathy known as Charcot-Marie-Tooth disease is a disorder of chronic peripheral neuropathy due to abnormal axonal structure and function. It has been recently shown that such patients including children are at increased risk for SDB (11,35). The pathophysiology is not clear and both phrenic nerve involvement leading to diaphragm weakness and pharyngeal neuropathy have been suggested.

Phrenic nerve paralysis—Paralysis of the phrenic nerve may result from injury during birth or during cardiothoracic surgery. Usually, phrenic nerve paralysis is unilateral and is associated with the radiological finding of an elevated hemi-diaphragm on the ipsilateral side. This condition may lead to hypoventilation during sleep.

Neuromuscular Junction

Myasthenia gravis—Myasthenia gravis (MG) is a chronic autoimmune disorder that results in progressive skeletal muscle weakness due to the presence of acetylcholine receptor antibodies at the neuromuscular junction. In early stages, the disorder affects extra-ocular, facial, and upper airway muscles. If untreated, MG could progress to a more general disease involving the diaphragm and may lead to respiratory failure.

Childhood forms include a congenital form and a transient neonatal form, found in about 20% of infants born to mothers with MG. The presence of SDB has not been well studied in these children. However, in adults, SDB is present in 36–60% of subjects (36,37). Both central and obstructive events are common and occur predominantly in rapid eye movement REM sleep. Risk factors for SDB are age, restrictive lung disease, diaphragmatic weakness and daytime alveolar hypoventilation. Pharmacotherapy with anticholinesterase medications and thymectomy have shown to improve the course of the disease and SDB significantly.

Muscle

Duchenne muscular dystrophy—Duchenne muscular dystrophy (DMD) is an x-linked disorder characterized by a defect in the dystrophin gene. The incidence is about 1:4000 males. The most important physiological correlates with longevity are: ambulation, progression of restrictive lung disease, and day time and nocturnal gas exchange.

Most of the information about SDB in children with NMD comes from studies describing DMD patients. Redding et al. (38) described 5 children with significant restrictive lung disease who presented with hypoventilation, poor sleep efficiency, and sleep fragmentation. Manni et al. (39) reported on nocturnal oxygen desaturations and mild hypoventilation in 6/11 non-ambulatory children with normal gas exchange during the day. Smith et al. (40) reported respiratory events including obstructive events and hypopnoeas in all 14 children with nine having significant oxygen desaturations. They found that respiratory events were more common in REM sleep. In a following study they demonstrated a significant drop in minute ventilation in this stage compared to NREM exposing the susceptibility to respiratory events in REM sleep (41). Their study also showed the lack of correlation between day time pulmonary function testing and SDB. In addition, these authors pointed out the difficulty distinguishing between true central apnoea from non-obstructive hypopnoea in these patients using chest and abdominal wall inductive plethysmography. They have suggested a careful analysis of simultaneous submental recordings to differentiate between the two (40).

The largest study on SDB in children with DMD is by Suresh et al. (8). This retrospective longitudinal study on 32 children with a median age of 8 years found that 31% had evidence of SDB. Interestingly, these authors noted a bimodal presentation of SDB with OSA more common in the first decade while hypoventilation more common in the beginning of the second

decade. The day time neurocognitive consequences of SDB in children with DMD are well described and show that these children have frequent day time somnolence, fatigue, and morning headaches (12).

Myotonic dystrophy—Myotonic dystrophy is a multi organ disease and the most common inherited muscle disorder affecting children and adults. It affects the muscles, brain, heart, gastrointestinal tract, lens, and reproductive organs. The incidence is 1:8000 births. Sleep disordered breathing has been reported in up to 34% of subjects and both central and obstructive respiratory events have been described (16,42). Children exhibit significant day time sleepiness associated with sleep fragmentation. However, in addition to respiratory related arousals it has been found that about a 1/3 of children have evidence of periodic limb movement during sleep leading to sleep fragmentation (6).

Mitochondrial myopathies—Mitochondrial myopathies are a group of neuromuscular diseases affecting the mitochondrial DNA content particularly in the cerebrum, nerves, and muscles. Some of the more common mitochondrial myopathies include the Kearns-Sayre syndrome, myoclonic epilepsy with ragged-red fibres, and the MELAS syndrome of mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes. Manni et al. (43) reported on SDB in 4 out of 8 patients with mitochondrial myopathies with ophthalmoplegia. Central apnoea and REM-related hypoventilation episodes were the most common manifestations found.

V. SLEEP EVALUATION

Symptoms of SDB may be subtle. The physician should especially be tuned to any of the following complaints: snoring, increasing numbers of nocturnal awakenings, daytime sleepiness, or morning headache that may be caused by cerebral vasodilation due to hypoventilation and CO₂ retention. Additional symptoms such as: fatigue, exertional dyspnoea, orthopnoea, swallowing difficulties, weakened cough, weight loss, and frequent respiratory infections with or without admissions, could suggest progressive of the underlying respiratory muscle disorder and worsening of nocturnal ventilation and SDB (12).

Daytime pulmonary function tests have typically been shown to correlate poorly with severity of SDB. However, several PFT findings warrant polysomnography: when FEV1 is below 40% predicted, base excess exceeds 4mmol/L, PaCO₂ is above 54mm Hg, and low day time SpO₂ is detected (9,12). Data obtained from polysomnography testing may be of significant value, not only to initiate therapy and improve quality of life for these patients but to alert to serious and even life threatening episodes. For example, it has been found that nocturnal SpO₂ nadir is one of the highest correlating measures associated with poor outcomes and survival rate in NMD subjects (9).

Although no consensus for evaluating SDB exists for children with all types of NMD, the American Thoracic Society has established a statement for patients with DMD (44). It suggests reviewing sleep quality and symptoms of SDB at every patient encounter. In addition, annual evaluation for SDB by polysomnography should be performed in patients starting from the time they are wheelchair bound and/or when clinically indicated. At times when full polysomnography is not readily available, both overnight pulse oximetry recording with continuous CO₂ monitoring or an unattended sleep study at home should be performed (7).

The evaluation of SDB and setting up non invasive ventilation (NIV) therapy should be performed in a sleep laboratory or a setting where sleep architecture, respiratory events, and gas exchange including CO₂ can be monitored and quantified (44). Serial evaluations are also

recommended for adjustment of ventilatory settings as the patient's requirements may change over time.

A comprehensive plan for following children with SDB has been suggested by Gozal (45). Accordingly, in addition to obtaining a full polysomnography every 6–12 months with pulmonary function tests, all children should undergo nutritional, cardiac, orthopaedic, and physical and occupational evaluations and review respiratory clearance technique, at similar intervals. In addition, social, psychological and educational needs for the child and their family should be addressed at each of these visits. Such follow up usually requires a multi disciplinary team for best results.

VI. TREATMENT AND OUTCOMES

The initial approach to treat NMD patients with SDB having either: central apnoea, obstructive apnoea, or gas exchange abnormalities due to hypoventilation, is to apply NIV during sleep. NIV has been shown to improve: nocturnal hypoxemia and hypoventilation, respiratory disturbance index, arousals, sleep architecture, heart rate, and day time sleepiness (5). In addition, it has been shown to preserve lung function and gas exchange during the day, reduce morbidly, improve QOL, and increase longevity (5,9). Some of the mechanisms by which NIV improves the above parameters are by: increasing upper airway stability during NREM and REM sleep, improving sleep efficiency, improving lung mechanics, normalizing blood gases, and reducing cardiac end diastolic volume.

The most common modality of NIV is bilevel positive airway pressure ventilation (BLPAP) using a nasal or full face mask interface. It can be effective and well tolerated even in very young infants (3,44). Continuous positive airway pressure ventilation (CPAP) should be used only in subjects with obstructive sleep apnoea in the absence of hypoventilation. As hypoxemia in these children is usually the result of hypoventilation, treatment with oxygen alone without concurrent supplemental ventilatory support should be avoided. Negative pressure ventilation should be used with caution due to the risk of precipitating upper airway obstruction. Invasive mechanical ventilation should be considered in patients with progressive respiratory failure and those with additional day time hypoventilation.

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Figure 1.

A 60 seconds recording during REM sleep of a 13 year old male with Duchenne muscular dystrophy demonstrating an obstructive apnoea (OA) event lasting 9 seconds. Note absence of flow in nasal pressure transducer (NPAF) while chest and abdomen paradoxical excursions continue. This event is associated with mild oxygen desaturation and mild hypoventilation with rise of end tidal to CO₂ to 51 mm Hg.

Figure 2.

A 60 seconds recording during REM sleep of a 14 year old male with Duchenne muscular dystrophy demonstrating obstructive hypoventilation (OH) event lasting 25 seconds. Note a reduction of flow in nasal pressure transducer (NPAF) while chest and abdomen paradoxical excursions continue. This event is associated with a mild oxygen desaturation and mild hypoventilation with rise of end tidal to CO₂ to 49 mm Hg.

Figure 3.

An 8½ hour hypnogram of the patient from Figure 2 demonstrating sleep stage transitions. Respiratory events include mostly obstructive hypopnoeas (OH). However, obstructive apnoeas (OA) and central apnoeas (CA) are also noted. Respiratory events are associated with oxygen desaturations and correlate with REM sleep (dark bars on upper panel). Persistent hypoventilation is evident by the high end tidal CO₂ recordings by capnography (CAP).

Table 1
Neuromuscular Disorders and Type of Sleep Disordered Breathing

(Modified with permission from reference 46). CA: central apnoea, OSA: obstructive sleep apnoea, MD: muscular dystrophy, MELAS: mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes

Level of involvement	Disorder	Muscles Involved	Sleep Disorder
Upper motor neuron	Cerebral palsy	Upper airway	OSA
Brainstem	Arnold Chiari type I & II	Upper airway, abdominals	CA
Spinal cord	C1-C2	Upper airway	OSA
	C3-C5	Diaphragm, intercostals, abdominals	Hypoventilation
	Below C6	Intercostals, abdominals	Hypoventilation
Motor neuron	Spinal muscular atrophy	Generalized	OSA, hypoventilation
	Poliomyelitis	Upper airway, abdominals, diaphragm	OSA, hypoventilation
Peripheral nerve	Hereditary motor and sensory neuropathies (Charcot-Marie-Tooth)	Upper airway, diaphragm	OSA, hypoventilation
	Hereditary sensory autonomic neuropathy	Upper airway	OSA, hypoventilation
	Phrenic nerve injury	Diaphragm	Hypoventilation
	Leukodystrophies	Generalized	Hypoventilation
	Guillain Barre	Generalized	Hypoventilation
	Polyneuropathy	Generalized	Hypoventilation
Neuromuscular junction	Congenital myasthenia	Generalized	Hypoventilation
	Myasthenia gravis	Generalized	OSA, hypoventilation
Muscle (Types)			
Dystrophinopathies	Duchenne MD, Becker MD	Generalized	OSA, hypoventilation
Nondystrophinopathies	Emery Dreifuss (rigid spine?)	Generalized, diaphragm	

Level of involvement	Disorder	Muscles Involved	Sleep Disorder
Myotonic dystrophy	Limb girdle MD	Diaphragm, intercostals, abdominals	Hypoventilation
	Fascioscapulohumeral	Upper airway, diaphragm	OSA, hypoventilation
	Merosin deficient	Generalized	OSA, hypoventilation
	Merosin positive	Upper airway	OSA, hypoventilation
	Myotonic dystrophy, congenital MD	Upper airway, diaphragm, decreased central drive	CA, OSA, hypoventilation
	Congenital myopathies	Nemaline, central core, centronuclear, multicore, minicore	OSA, hypoventilation
Metabolic myopathies	Glycogenoses	Upper airway, diaphragm	OSA, hypoventilation
Mitochondrial myopathies	Mitochondrial myopathy with ophthalmoplegia, MELAS	Generalized, decreased central drive	CA, OSA, hypoventilation
Inflammatory myopathies	SLE, polymyositis	Generalized, diaphragm	Hypoventilation