AANEM

News Science Anthology

Journal Article Summaries From the AANEM News Science Editorial Board (NSEB) | January-December 2024

News Science Editorial Board

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2023-2024 NSEB

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Jan. 10, 2024

Citation: Ludolph A, Dupuis L, Kasarskis E, et al. Nutritional and metabolic factors in amyotrophic lateral sclerosis. *Nat Rev. Neurol.* 2023 Sep;19(9):511-524. DOI: 10.1038/s41582-023-00845-8. PMID: 37500993.

Submitted by: Marcus Pai, MD
Edited by: Joshua Wilson, MD

Summary: Weight loss and metabolic abnormalities are common in patients with amyotrophic lateral sclerosis (ALS), often preceding symptom onset and predicting poorer outcomes. Clinical studies show premorbid weight loss, low body mass index, and loss of fat mass are associated with increased ALS risk and faster progression. Metabolic alterations such as reduced adiposity and cholesterol can be detected years before symptoms arise, indicating a causal role in disease pathogenesis rather than just a consequence of impairment.

At the cellular level, ALS mutations directly disrupt metabolism and mitochondrial function. Mutant SOD1, TDP-43, FUS, and C9orf72 proteins impair bioenergetics in motor neurons, astrocytes, and skeletal muscle. These impairments contribute to energy depletion in metabolically demanding neurons, promoting degeneration. Systemically, mitochondrial dysfunction likely underlies the hypermetabolism observed in up to 68% of patients with ALS, where resting energy expenditure exceeds intake.

Preclinical models and early human trials suggest that nutritional interventions and compounds targeting cellular metabolism may be therapeutic in ALS. High-calorie diets extend survival in mice, while nutritional supplements appear to slow progression and reduce neurofilament levels in ALS patients. Drugs improving mitochondrial function and antioxidant pathways also show promise. Optimizing energy balance through diet alongside targeted metabolic treatments represents a promising dual approach to slowing disease progression.

Comments: This review provides a compelling look at the role of nutrition and metabolism in ALS; some limitations should be noted. The causes of hypermetabolism remain unclear, with the authors acknowledging that further research is needed to elucidate mechanisms. Human trials of nutritional interventions are still in the early phases, with optimal caloric intake and composition not yet defined. These trials' small sample sizes and short durations limit conclusions about long-term impacts on disease progression. Larger, longer studies will be essential to validate preliminary findings. The implications of this research are exciting. The evidence linking premorbid weight loss to ALS risk suggests a window for early intervention exists years before the onset of weakness. This raises the possibility that weight maintenance or metabolic treatments in high-risk individuals could help delay or prevent disease onset. The preclinical efficacy of nutritional and bioenergetic approaches also provides hope for slowing progression by enhancing energy supply and mitochondrial function in patients with ALS.

Feb. 7, 2024

Citation: Buitenhuis SM, Pondaag W, Wolterbeek R, Malessy MJA. Tactile perception of the hand in children with an upper neonatal brachial plexus palsy. *Arch Phys Med Rehabil.* 2023;104(6):872-877. doi:10.1016/j.apmr.2022.11.010

Submitted by: Rebecca O'Bryan, MD
Edited by: Nandita Keole, MD

Summary: The aim of this study was to investigate sensory deficits that cause impairment of hand function in children between 7-12 years with an upper neonatal brachial plexus palsy (NBPP). This was a cross-sectional study comparing 41 children with upper NBPP in non-dominant hand with 25 healthy controls (mean ages approximately 10 yo). All children had normal hand motor function as evaluated by routine clinical examination. A monofilament was used to assess sensation in the fingertips along the radial and ulnar sides. The ability to localize stimuli on the tips of the fingers in children with an upper NBPP was significantly diminished in all fingers, except for the little finger, as compared with healthy controls. Mean localization scores were 6.6 (thumb) and 6.3 (index finger) in the NBPP group and 7.6 in both fingers for controls (maximum score possible is 8.0). Localization scores were significant lower in regions attributed to dermatomes C6 (P=0.115)

Comments: This article focuses on hand function in children affected with upper trunk BP, and notes that decreased sensation in all but the 5th digit persists and may affect hand function. They suggest sensory focused therapy for these children to improve their functional status. Outcome focus in upper trunk brachial plexopathy is usually on the proximal motor function, which can be severely affected in these children, but care should be taken not to ignore sensation deficits that may involve the hand as well.

Feb. 21, 2024

Citation: Hutin E, Ghédira M, Vinti M, Tazi S, Gracies JM, Decq P. Comparing the effect of implanted peroneal nerve stimulation and ankle-foot orthosis on gait kinematics in chronic hemiparesis: A randomized controlled trial. *J Rehabil Med.* 2023;55:jrm7130. Published 2023 Aug 7. doi:10.2340/jrm.v55.7130

Submitted by: Joshua Wilson, MD
Edited by: Nandita Keole, MD

Summary: Following a central nervous system (CNS) insult, the resulting spastic gait pattern is often characterized by impaired dorsiflexion. This limitation is most noticeable during the swing phase, resulting in reduced foot clearance, posing an increased tripping hazard, and decreased efficiency. Multiple factors are believed to contribute, including dorsiflexor weakness, plantar flexor spasticity, and co-contraction dyssynergy. Traditionally, this has been corrected with ankle foot orthotic (AFO) that passively positions the ankle in neutral and only works to address the latter two factors. The study at hand investigated the effects of semi-implanted selective functional electrical stimulation (SIS-FES) on gait kinematics compared to AFOs. In a controlled study, participants (n=27) were randomized to either the AFO or SIS-FES group. Subjects were required to have passive dorsiflexion to a neutral position and be able to ambulate a minimum of 50 meters with or without an assistive device. Gait mechanics were recorded two months before device implantation of a STIMuSTEP or AFO fitting and again at three and six months. At each assessment, three sets of measurements were collected with a stimulator or AFO off, then on, and finally off again. The primary outcome was walking speed, but due to multiple secondary outcomes, a Bonferroni correction factor was used. At the three-month follow-up, there was a non-significant difference between groups after turning on stimulation or donning AFOs in terms of walking speed, cadence, bilateral step length, ankle dorsiflexion amplitude, and knee flexion amplitude ($p>0.05$). There was, however, a significant decrease in mean dorsiflexion speed after taking off the AFO that was not observed in the SIS-FES group (AFO: OFF, 11.4±9.1°/s, ON, 4.6± 4.7°/s, $p = 0.02$; SIS-FES: OFF, 13.9 ± 8.8°/s, ON, 13.7± 8.8°, $p>0.05$). The impact of training was evaluated by comparing gait kinematics at three and six months while subjects used their AFO or with SIS-FES turned on. No significant difference was observed between groups or over time (all $p>0.05$). The therapeutic benefit was evaluated by comparing gait mechanics before implantation or AFO fitting and again at three and six months without using the respective devices. While there was a significant increase in maximal knee flexion, it was only 2° ($p=0.03$), and no significant difference was seen between groups. ($p>0.05$). The overall impact of device use was evaluated by comparing gait kinematics at baseline to those at six months while using their respective devices. While SIS-FES showed significant speed increases (+0.10 m/s, $p=0.03$), cadence (+0.09 steps/s, $p=0.006$), maximum dorsiflexion (+5°, $p=0.0002$) and mean knee flexion speed (+11°/s, $p=0.04$); there was no significant difference when compared to those with AFOs.

Comments: While the authors of the study point to retained average dorsiflexion speed after turning off stimulation compared to a drop in speed after AFO removal, the results of SIS-FES were overall underwhelming. The improvements seen from the immediate activation of SIS-FES were similar to those obtained by using an AFO. In both groups, there was no observed improvement in training with either device after stopping each device, except for a modest increase in knee flexion. Even after six months of use, the improvements seen with SIS-FES were matched by using an AFO. While SIS-FES has the apparent benefit of stimulating dorsiflexion, its magnitude of effect on paretic muscle seems to have minimal impact on the overall gait mechanics of the lower extremity. It is possible that other factors, such as plantar flexion spasticity and/or co-contraction dyssynergia, may be dampening the impact of FES. However, this will require further investigation to elucidate.

March 6, 2024

Citation: Suslov VM, Lieberman LN, Carlier PG, et al. Efficacy and safety of hydrokinesitherapy in patients with dystrophinopathy. *Front Neurol.* 2023;14:1230770. Published 2023 Jul 26. doi:10.3389/fneur.2023.1230770

Submitted by: Nakul Katyal, MD
Edited by: Joshua Wilson, MD

Summary: This study aimed to assess the effectiveness and safety of regular pool dynamic aerobic exercises in ambulatory patients with Duchenne muscular dystrophy (DMD). Outcome measures, including the six-minute walk test, rising time from the floor, 10-meter running, stair climbing and descending, and muscle strength of the upper and lower extremities, were assessed at baseline and during dynamic observation at two and four months. In addition, a quantitative muscle MRI of the pelvic girdle and thigh was performed before and after training during the course. The aquatic rehabilitation course was divided into preparatory and training phases. Each patient's training intensity was individualized depending on their functional heart reserve. Each session lasted 60 min with a frequency of three times a week.

Twenty-eight patients with genetically confirmed DMD were included in the study. The average participant age was 6.9 ± 0.2 years. To be included all patients had to be independent in mobility. Further all patients were on daily steroid according to DMD Care consideration.

There were statistically significant improvements in multiple outcomes four months post-training compared to baseline, including the six-min walk test (462.7 ± 6.2 m vs 492.0 ± 6.4 m), rising-from the-floor test (4.5 ± 0.3s vs. 3.8 ± 0.2 s), 10-meter-running test (4.9s ± 0.1 vs. 4.3 ± 0.1 s); four-stair climbing test (3.7 ± 0.2 vs. 3.2 ± 0.2 s) and four-stair descent test (3.9 ± 0.1 s vs. 3.2 ± 0.1 s). Quantitative MRI analyses showed that the T2 water content of muscles remained constant during the study. Eighteen patients experienced mild side effects, including muscle pain (12 patients), muscle tension, and hardening in the lower extremities (13 patients). All patients were able to continue the course.

Comments: Currently, there is a lack of consensus guidelines regarding a safe and efficient exercise regimen for patients with DMD. This research emphasized the efficacy of dynamic aerobic exercises in a pool setting for ambulatory DMD patients. It demonstrated improvements in timed function tests with no significant alterations in muscle water content, suggesting aquatic kinesiotherapy's safety for individuals with dystrophinopathy. This study contributes to the limited body of literature regarding the effectiveness of aquatic aerobics for those with neuromuscular disorders. Additional research is imperative to assess the long-term impacts of these exercises in dystrophinopathies and the rate of disease progression. This article is relevant to the AANEM audience because NM and PM&R physicians provide care for patients with dystrophinopathies. Developing a safe and efficient exercise regimen for these patients is crucial to mitigate disease advancement and related orthopedic issues.

Article of Similar Interest: Huguet-Rodríguez M, Arias-Buría JL, Huguet-Rodríguez B, Blanco-Barrero R, Braña-Sirgo D, Güeita-Rodríguez J. Impact of Aquatic Exercise on Respiratory Outcomes and Functional Activities in Children with Neuromuscular Disorders: Findings from an Open-Label and Prospective Preliminary Pilot Study. *Brain Sci.* 2020;10(7):458. Published 2020 Jul 17. doi:10.3390/brainsci10070458

March 20, 2024

Citation: Markvardsen LK, Sindrup SH, Christiansen I, Sheikh AM, Holbech JV, Andersen H. Standardized tapering off subcutaneous immunoglobulin in chronic inflammatory demyelinating polyneuropathy. *J Neuromuscul Dis*. 2023;10(5):787-796. doi:10.3233/JND-221615

Submitted by: Pritikanta Paul, MD
Edited by: Joshua Wilson, MD

Summary: Around one-third of chronic inflammatory demyelinating polyneuropathy (CIDP) patients experience symptom remission over time, making it advisable to regularly attempt reducing or discontinuing immunoglobulin treatment to detect clinical remission. Early identification of remission can lead to reduced treatment costs and fewer side effects. However, there is still a gap in understanding of how to safely and effectively taper off this treatment, particularly with subcutaneous immunoglobulin (SCIG).

The objective of this study was to determine the frequency of CIDP patients who entered remission after complete discontinuation of treatment with SCIG by employing a standardized tapering-off regimen. The study was conducted from March 2018 to June 2022, recruiting participants from four Danish neurological departments. Patients followed a stepwise tapering regimen, reducing the initial SCIG dose by 90%, 75%, 50%, 25%, and 0% every 12 weeks if no deterioration occurred. Clinical evaluation included disability scores, quality of life assessments, grip strength, and manual muscle testing using the Medical Research Council scoring. The clinical criteria for deterioration included an increase in disability scores or a decrease in grip strength.

Of the 55 patients enrolled with stable disease, 36% (N=20) successfully stopped SCIG without relapse. Of the remaining 35 participants who experienced relapse during the tapering process, 7 (13%) could not tolerate any dosage reduction, while 11 (20%) tolerated a 10% reduction, 13 (24%) tolerated a 25% reduction, and 3 (5%) tolerated a 50% reduction. One participant (2%) experienced deterioration after discontinuing treatment but recovered when treated with a 25% dosage. Patients who experienced relapse were more likely to have a higher baseline dosage of SCIG. Of those who relapsed, 97% could be stabilized by increasing SCIG to the last given dose prior to deterioration, with a median dose reduction of 10%.

After 2 years, 90% of patients who discontinued SCIG remained in remission. Additionally, frequent clinical evaluation every 6 weeks did not significantly improve deterioration detection compared to less frequent evaluation (every 12 weeks). This study concluded that SCIG can be tapered off effectively in stable CIDP patients.

Comments: This study offers valuable insights into the gradual reduction of SCIG treatment in CIDP. A vast majority of AANEM audience are care providers for patients with CIDP and this study investigates treatment outcome with SCIG.

April 3, 2024

Citation: Levison LS, Thomsen RW, Andersen H. Hospital-diagnosed morbidities and recent surgery as risk factors for developing Guillain-Barré syndrome. *Eur J Neurol.* 2023;30(10):3277-3285. doi:10.1111/ene.15955

Submitted by: Justin Willer, MD
Edited by: Joshua Wilson, MD

Summary: This study investigated the association between Gillian-Barré syndrome (GBS) development, hospital-associated morbidity, and recent surgery.

Over a 13-year period, 1,086 GBS cases and 10,747 matched controls were identified. The frequency of infection was compared to controls (34.3% versus 17.0%).

Matched odds ratio showed strongest associations with leukemia (OR = 4.59, 95% CI = 1.74–12.08), lymphoma (OR = 2.09, 95% CI = 0.97–4.49), diabetes (OR = 2.12, 95% CI = 1.44–3.12), moderate to severe liver disease (OR = 1.98, 95% CI = 0.68–5.80), myocardial infarction (OR = 1.73, 95% CI = 1.20–2.49), congestive heart failure (OR = 1.62, 95% CI = 1.08–2.44), and cerebrovascular disease (OR = 1.62, 95% CI = 1.21–2.16).

Surgical procedures within 5 months prior were noted in 10.6% of cases and 5.1% of controls (OR= 2.2). The risk of developing GBS was greatest during the first-month post-operative period.

This study has clear limitation being retrospective having matched controls. It further only establishes and association and not a causal link between risk factor and development of GBS.

Comments: Interestingly, we tend to think of GBS in patients with acute infections and critical illness polyneuropathy/ myopathy in patients with severe and debilitating medical conditions. Based on the results of this study, we may need to step back and look at the risk factors that may play a role in putting a patient at a greater risk of developing GBS.

OR = odds ratio, CI = confidence interval

April 17, 2024

Citation: Castiglione JI, Crespo JM, Bendersky M, et al. Guillain-Barré syndrome and COVID-19 vaccine: A multicenter retrospective study of 46 cases. *J Clin Neuromuscul Dis.* 2023;25(1):1-10. doi:10.1097/CND.000000000000043.

Submitted by: Pritikanta Paul, MD
Edited by: Joshua Wilson, MD

Summary: In recent times, there has been growing concern about a potential association between adenovirus vector COVID-19 vaccines and an increased risk of Guillain–Barré syndrome (GBS). This study investigated the clinical and electrophysiological characteristics of cases of GBS occurring after COVID-19 vaccination and compared them to GBS cases unrelated to recent vaccination.

The study included 91 cases of GBS from March 2020 to March 2022 in Buenos Aires, Argentina. Forty-six of the 91 individuals had received SARS-CoV-2 (COVID-19) vaccination within the 4 weeks preceding the onset of symptoms and were classified as having vaccine-associated GBS. While four vaccine formulations were reported, two adenovirus-based vaccines, Sputnik V [Gam-COVID-Vac] and AstraZeneca [ChAdOx1-S], were associated in 93.3% of cases. These two vaccines, according to WHO data, make up less than 7% of vaccines given since start of the pandemic.

Only cranial nerve palsies and bilateral facial paralysis were significantly more common in the postvaccination group. No significant differences were detected in other clinical findings, including cerebrospinal fluid studies, neurophysiological aspects, hospital stay duration, mortality rates, or response to treatment. Throughout the follow-up period, both groups displayed favorable improvements in GBS disability scores at the 3-month evaluation, and there were no instances of relapse.

Among the vaccine-associated GBS group, 11 out of 46 received additional COVID-19 vaccine boosters with no adverse events reported. It should be noted that most vaccine associated GBS cases had initially received adenoviral vector vaccines (45 out of 46), while boosters were all mRNA vaccines. The authors acknowledge that the study's limitations include a retrospective nature and observer bias.

Comments: While this study did not investigate a causative link between COVID-19 vaccines and GBS, its comparative analysis offers valuable insights into the clinical and electrophysiological features of GBS cases occurring shortly after vaccination. Larger-scale studies and continuous monitoring are necessary to determine if an association exists. The connection between vaccines and GBS is an exceptionally intriguing subject in clinical practice. The AANEM audience frequently tends to GBS patients or is engaged in clinical research and relevant practices related to this.

May 1, 2024

Citation: Raj K, Radhakrishnan DM, Bala P, et al. Electrophysiology and magnetic resonance neurography findings of nontraumatic ulnar mononeuropathy from a tertiary care center. *J Clin Neuromuscul Dis.* 2022;24(2):61-67. doi:10.1097/CND.0000000000000419

Submitted by: Oksana Sayko, MD
Edited by: Rebecca O'Bryan, MD

Summary: The ulnar nerve is frequently involved in mononeuropathies of the upper limb. Ulnar neuropathies have been diagnosed conventionally using clinical and electrophysiological findings. Physicians opt for nerve imaging in patients with ambiguous electrophysiological tests to gain additional information, identify etiology and plan management.

In this study the authors described the electrophysiological and the magnetic resonance neurography (MRN) findings in patients with nontraumatic ulnar neuropathy.

Thirty-nine patients with suspected nontraumatic ulnar mononeuropathy were recruited; clinical assessment and electrophysiological studies (EPSs) were done in all. After EPS, patients with localization of lesion along the ulnar nerve underwent MRN.

All 39 patients recruited had clinical findings suggestive of ulnar neuropathy; Electrophysiological confirmation was possible in 36/39 (92.30%) patients. Localization of ulnar nerve lesion to elbow and wrist was possible in 27 (75%) and 9 (25%) patients, respectively. MRN was done in 22 patients; a lesion was identified in 19 of 22 (86.36%) ulnar nerves studied. Thickening and hyperintensity in T2 W/short TI inversion recovery images of ulnar nerve at the level of olecranon, suggesting ulnar neuropathy at elbow, was the commonest (8/22) imaging findings.

The authors concluded that MRN acts as a complimentary tool to EPS for evaluating nontraumatic ulnar neuropathy. By identifying the etiology, MRN is likely to modify the management decision.

Comments: This study describes another method of diagnosing nontraumatic ulnar neuropathy that is complimentary to EMG and may be used in the diagnostically difficult cases. Ulnar neuropathy is a common neuropathy seen in EMG lab that is sometimes difficult to localize based on the electrodiagnostic findings alone.

May 15, 2024

Citation: Juříková L, Masárová L, Panovský R, Pešl M, Revendová KŽ, Volný O, Feitová V, Holeček T, Kincl V, Danhofer P, Voháňka S, Haberlová J and Podolská K (2024) Decreased quality of life in Duchenne muscular disease patients related to functional neurological and cardiac impairment. *Front. Neurol.* 15:1360385.

Submitted by: Nakul Katyal, MD
Edited by: Milvia Pleitez, MD

Summary: This prospective study involved 37 patients 8 years and older who were diagnosed with Duchenne muscular dystrophy (DMD). The authors assessed the impact of both neurological and cardiac factors on quality of life (QoL) utilizing the PEDSQL 3.0 and EQ-5D questionnaires.

The PEDSQL 3.0 Neuromuscular Module questionnaire, specifically designed for children, focuses on aspects such as neuromuscular disease impact, communication challenges, and family resources. The EQ-5D questionnaire comprises inquiries regarding mobility, self-care, daily activities, discomfort, anxiety, and overall health status.

Neurological status evaluation encompassed factors like ambulatory ability, need for assistance in sitting, and presence of scoliosis, including any history of corrective surgery. Upper limb mobility was assessed across five categories ranging from preserved mobility to reliance on assistive devices for tasks such as using a touchpad or mouse. Additionally, demographic information, current medication regimens, and comorbid conditions were recorded.

Participants were stratified into three age groups: 8–12 years, 13–18 years, and adult patients. Younger individuals completed the PEDSQL 3.0 questionnaire, while adults filled out the EQ-5D. Both DMD patients and their parents completed the PEDSQL 3.0 questionnaire.

Following a baseline assessment, patients underwent a neurological examination and subsequently completed the questionnaire on the same day. Cardiac magnetic resonance imaging (MRI) was performed within a week of the neurological evaluation.

The study revealed a negative relationship between upper limb movement and various aspects of daily function including overall mobility, self-care, and usual activities. Statistically significant differences were observed in total mobility, self-care, daily activities, and perceived well-being when comparing ambulatory versus non-ambulatory DMD patients, as well as sitting versus non-sitting individuals.

DMD patients receiving ACE inhibitors or sartans exhibited better overall mobility compared to those without such therapy. Furthermore, upper limb movement demonstrated a positive correlation with septal mitral annular plane systolic excursion (MAPSE), indicating a relationship between upper limb function and cardiac performance. However, no significant associations were detected between MAPSE and anxiety or depression levels.

Comments: This prospective study provided a comprehensive assessment of the QoL in DMD patients across different age groups and levels of disability, in relation to functional neurological and cardiac impairment.

The authors observed that improved upper limb movement was linked to better overall mobility and emotional well-being, although QoL showed negative correlations with upper limb movement. Additionally, cardiac parameters were found to be interconnected with motor function. Variations in QoL were evident among ambulatory/non-ambulatory and sitting/non-sitting DMD patients.

A major limitation of the study was its small sample size and reliance on data from a single center. Further research

investigating QoL in DMD is warranted to validate these findings. Despite these limitations, the results underscore the importance of implementing personalized care strategies in managing DMD patients.

Both neurologists and PM&R offer treatment to patients with DMD. It's crucial to understand how cardiac and neurological issues affect the quality of these patients to ensure they receive the best possible care.

Article of similar interest: Kohler M, Clarenbach CF, Böni L, Brack T, Russi EW, Bloch KE. Quality of life, physical disability, and respiratory impairment in Duchenne muscular dystrophy. *Am J Respir Crit Care Med.* (2005) 172:1032–6. doi: 10.1164/rccm.200503-322OC

May 29, 2024

Citation: Qavi A, Jasrotia RB, Maurya PK, et al. Autonomic function tests, heart rate variability, and electrophysiological evaluation in patients with a primary episodic headache: An observational study. *J Clin Neurophysiol.* 2023;40(7):625-633. doi:10.1097/WNP.0000000000000943

Submitted by: Eman Tawfik, MD
Edited by: Rebecca O'Bryan, MD

Summary: The basic postulated mechanism of headache involves the activation of the trigeminovascular system and sensitization of trigeminal brainstem nuclei. However, autonomic nervous system dysfunction has been reported in various headache disorders and proposed as one of the mechanisms that may trigger the headache attacks.

This cross-sectional study aimed to evaluate the parasympathetic and sympathetic autonomic functions in patients with migraine and tension-type headache. During the period from June 2018 to June 2020, the authors enrolled 100 patients in the age group of 14-50 years who have episodic migraine and episodic tension-type headache according to the International Classification of Headache Disorder third edition beta. They excluded patients with systemic illness such as DM, HTN, hypothyroidism and patients with previous cranial neuropathy, Bell palsy, facial trauma, and leprosy. The study also included 50 healthy age- and sex-matched controls.

Electrophysiological and autonomic function tests were performed in all patients during headache-free periods at least 7 days after headache to avoid the effect on ictal and postdromal sympathovagal tone. At the time of the tests, the patients were off from any prophylactic drugs for two or more weeks and were also not taking any abortive/acute treatment of headache on the day of the test. Electrophysiological tests included blink Reflex and sympathetic skin response (SSR). Parasympathetic function tests included heart rate responses to deep breathing, to Valsalva maneuver, and to standing. The sympathetic function tests included blood pressure responses to the sustained handgrip test and to standing. Based on these 5 autonomic tests, the patients were classified into normal, early, definite, severe, and atypical according to the Ewing Classification of Autonomic Failure.

Parasympathetic and sympathetic dysfunction was found in the patients group. Significant difference in blood pressure response to sustained handgrip and heart rate response to Valsalva maneuver was found in patients with migraine. Significant difference in blood pressure response to sustained handgrip and heart rate variability was found in patients with a tension-type headache. The blink reflex test and SSR were normal, but the latency of the SSR was significantly prolonged in patients compared to the controls. Patients with migraine showed a significant dysautonomia in category three of the Ewing battery for autonomic functional disability.

Comments: The study adds to our understanding of the autonomic changes that may occur in patients with episodic primary headache (migraine and tension-type headache). It included many patients and assessed both sympathetic and parasympathetic functions. However, the authors did not assess the patients during the attack which did not allow the study of the effect of treatment on autonomic dysfunction and the relation between the severity of autonomic dysfunction and headache severity. Episodic primary headache is very common worldwide. It impacts the patient's quality of life and imposes a financial load on the health care system. Understanding the underlying mechanisms may help the physicians better treat the patients.

Articles of Similar Interest:

1. Azam MA, Katz J, Mohabir V, Ritvo P. Individuals with tension and migraine headaches exhibit increased heart rate variability during post-stress mindfulness meditation practice but a decrease during a post-stress control condition - A randomized, controlled experiment. *Int J Psychophysiol.* 2016;110:66-74. doi:10.1016/j.ijpsycho.2016.10.011

2. Miglis MG. Migraine and autonomicdDysfunction: Which is the horse and which is the jockey?. *Curr Pain Headache Rep.* 2018;22(3):19. Published 2018 Feb 23. doi:10.1007/s11916-018-0671-y

June 12, 2024

Citation: Bach JR, Saporito L, Weiss W. Spinal muscular atrophy type 1 survival without new pharmacotherapies: Two treatment paradigms. *Am J Phys Med Rehabil.* 2024;103(3):233-237. doi:10.1097/PHM.0000000000002354

Submitted by: Nandita Keole, MD
Edited by: Milvia Pleitez, MD

Summary: This is an observational study that aims to present noninvasive respiratory management outcomes using continuous positive pressure noninvasive ventilatory support (CNVS) and mechanical in-exsufflation (MIE) from infancy for spinal muscular atrophy (SMA) type 1. Additionally, the study looks at the outcomes and bearing on new medical therapies.

Noninvasive ventilatory support was begun for consecutively referred symptomatic infants with SMA type 1 from 1 to 10 months of age. Intercurrent episodes of respiratory failure were managed by intubation then extubation to CNVS and MIE despite failing ventilator weaning and extubation attempts. Intubations, tracheotomies, and survival were monitored.

Results: Of 153 patients with SMA type 1 consecutively referred since 1995, 37 became CNVS dependent, almost half before 10 years of age. Of the 37, 18 required CNVS for a mean 18.6 ± 3.3 years to a mean 25.3 (range, 18–30) years of age, dependent from as young as 4 months of age with 0 to 40 ml of vital capacity. One of the 18 died from COVID-19 acute respiratory distress syndrome at age 24 after 23 years of continuous noninvasive ventilatory support. Extubation success rate of 85% per attempt (150/176) resulted in only one undergoing tracheotomy.

Conclusions: Medical treatments begun during the first 6 weeks of age convert SMA 1 into SMA type 2 or 3, but cough flows remain inadequate to avoid many pneumonias. The pneumonias when resolved by a treatment paradigm of extubation to CNIVS and MIE, eliminate the need to resort to tracheotomies. The regimen of NVS and MIE prevent perhaps 90%, but not all pneumonias or need for intubations. However, even when SMA1 CNVS users are ventilator unweanable for months to years before requiring intubation for pneumonia or general anesthesia, they can almost invariably be extubated back to CNVS and MIE. With or without gene therapy or other upstream medications for SMA, cough flows remain suboptimal and result in URI-pneumonias and intubations. Since 2018 the practice has only had three patients (who were treated with the newer medications) referred that were intubated and unweanable. After successful extubations to CNVS, however, all three returned to their states. They subsequently died when NVS and MIE were not available to them.

Comments: This paper refers to appropriate use of MIE and CNVS to help patients with lower vital capacity maintain survival. It highlights the need to properly use an available modality of treatment appropriately to help keep SMA type 1 alive without the need for tracheostomies. This is something even more important in cases when tracheostomies are declined by the families.

June 26, 2024

Citation: Haig AJ, McGuire TJ. Anatomical study and proposed EMG technique for the cervical paraspinal muscles. *PM R.* 2024;16(2):165-173. doi:10.1002/pmrj.13046

Submitted by: Oksana Sayko, MD
Edited by: Rebecca O'Bryan, MD

Summary: Paraspinal EMG has proven to be the most sensitive component of the EDX examination for lumbar spinal disorders. However, no standardized, anatomically validated technique has been proposed for the cervical region. The purpose of this paper is to take the first step in improving the diagnostic power of cervical EMGs by presenting a standardized cervical EMG technique and scoring system based on the current textbook understanding of cervical spinal anatomy and clinical experience. The anatomical study focuses specifically on the multifidus muscle, which may be innervated by specific single nerve roots as found in previous studies of the lumbar multifidus muscles.

A library search found 32 anatomy texts published between 2000 and 2021. Of these, 11 were unique and appropriate. Most texts described the basic muscle anatomy similarly, but only one cited original research.

Most anatomy texts agree on some generalities but fail to agree on finer details such as the number of levels the multifidus spans (two to five, two to four, three) or the precise attachment points in the different sections of the spine (transverse process or articular process). These are crowded into a small area between the spinous processes and transverse processes.

Based on the understanding of reviewed textbook resources, the authors proposed a cervical paraspinal mapping technique that involves skin insertions from 1 to 2 cm lateral to the C5, C7, and T2 spinous processes. The needle samples transversely and deep toward midline, contacts bone, then is withdrawn and redirected to sample medial and caudally to midline to bone, creating two scores of 0–4 at three levels, theoretically resulting in scores of 0–24.
The author admits that the targeted muscle is small and deep. It is deep under other muscles and a specific fascicle of the muscle, potentially innervated by only one posterior primary ramus, may be only a few millimeters thick. EMG of the cervical paraspinals that does not target this small space between the spinous process and the transverse process is likely to miss all of the muscle, and even within that space one cannot be confident that the intended root-specific fascicle has been sampled. This is in contrast to the relatively large lumbar multifidus, which is mostly not overlapped by other muscles.

This technique must be validated by clinical research to determine the range of normal, reproducibility, and the spectrum of findings in various disorders.

Comments: This article proposes a method of potentially more reliable diagnosis and localization of cervical radiculopathy based on paraspinal muscles sampling. Cervical radiculopathy is a common pathology seen in the EMG lab. More precise localization may add to more specific treatment.

July 10, 2024

Citation: Falco P, Galosi E, Giulia Di Stefano, et al. Autonomic small-fiber pathology in patients with fibromyalgia. *The journal of pain/Journal of pain*. 2024;25(1):64-72. doi:https://doi.org/10.1016/j.jpain.2023.07.020

Submitted by: Rebecca O'Bryan, MD
Edited by: Milvia Pleitez, MD

Summary: The aim of this study was to investigate whether small fiber pathology (termed SFP) associated with fibromyalgia shows evidence of damage to dermal autonomic nerve fibers, and how the damage is associated with autonomic symptoms. A total of 138 patients participated (58 patients with fibromyalgia syndrome (23 diagnosed with SFP), 48 healthy subjects, and 32 patients with diabetic or transthyretin familial amyloid small fiber neuropathy (SFN). Skin biopsy was performed to investigate intraepidermal nerve fiber density, piloerector muscle and sweat gland nerve fiber density (SGNFD). These findings were correlated with autonomic symptoms using the Composite Autonomic Symptom Score 31 question questionnaire. NCSs were performed to ensure no large fiber neuropathy was present. Diagnosis of pure SFN relied on normal NCS parameters and fulfilled the Besta criteria. These criteria are based on having at least two abnormal findings among the three commonly used to assess small-fiber damage. The criteria include, the presence of two negative clinical signs (pinprick and thermal sensory loss), possibly associated with positive clinical signs (allodynia and/or hyperalgesia), abnormal warm and/or cold thresholds at the foot as assessed with quantitative sensory testing, and reduced intraepidermal nerve fiber density (IENFD) at the distal leg. Results were notable for findings that the piloerector muscle and SGNFD were lower in patients with fibromyalgia associated SFP than that in healthy subjects. However, autonomic small-fiber damage had no correlation with autonomic symptoms severity. In patients with SFP, the intraepidermal, piloerector muscle, and SGNFD were higher than that in patients with small-fiber neuropathy.

Comments: This is an interesting study looking at small fiber neuropathy in patients with fibromyalgia. However, the method of selecting patients with SFP utilizing IENFD, then utilizing that specific group to investigate differences with healthy controls would seem to potentially bias findings specifically looking for evidence of autonomic nerve fiber damage. At best, this study shows a correlation between the presence of IENFD and that of muscle and SGNFD. This is a novel finding and does further indicate that a subset of patients with fibromyalgia have pathology associated with autonomic nerve fibers. The significance of this remains to be seen given the lack of correlation with symptoms. Understanding the underlying pathology as it relates to the peripheral nervous system is relevant. This study is a very small sample size, even smaller when those without SFP are selected out, and more research is needed.

July 24, 2024

Citation: Di Pietro G, Cioffi E, Falco P, et al. Nerve ultrasound in Friedreich's ataxia: Enlarged nerves as a biomarker of disease severity. *Clin Neurophysiol*. 2024;159:75-80. doi:10.1016/j.clinph.2024.01.004

Submitted by: Eman Tawfik, MD
Edited by: Rebecca O'Bryan, MD

Summary: Friedreich's ataxia affects the central and peripheral nervous systems, as well as other systems. There is a continuous search for effective treatment. Therefore, finding a reliable disease biomarker is needed.

Sensory neuropathy is one of the disease hallmarks. Nerve conduction studies (NCSs) are typically used to detect neuropathy but is not the optimum biomarker because sensory responses are commonly lost. Therefore, the authors in this study assessed the ability of nerve ultrasound (US) to serve as a potential biomarker in patients with Friedreich's ataxia.

The authors prospectively recruited patients who were genetically confirmed to have Friedreich's ataxia.

Motor NCS of the median, ulnar, tibial, and peroneal nerves and sensory NCS of the median, ulnar, superficial radial, and sural nerves were performed for all patients. The median, ulnar, tibial, peroneal, and sural nerves were scanned along their entire course and the nerve cross-sectional area (CSA) was measured at pre-determined levels. The total number of abnormal sites was determined after exclusion of the common entrapment sites.

There were 10 patients with Friedreich's ataxia and 20 healthy controls included. Nine patients had lost sensory responses and one patient had reduced amplitude of the sensory responses in NCS. The motor NCS were completely normal.

Significant enlargement of the median and ulnar nerves at the axilla and arm was found in the patients group compared to the controls. The total number of abnormal nerve sites positively correlated with the Scale for the Assessment and Rating of Ataxia (SARA), Friedreich's Ataxia Rating Scale (FARS), modified FARS (mFARS), the Inflammatory Neuropathy Cause and Treatment Disability Score (INCAT), and the Activities of Daily Living (ADL 0-36 score), but inversely correlated with the Instrumental Activities of Daily Living (IADL).

The correlation between nerve US abnormalities and the clinical disability scales denotes a potential role of nerve US as a biomarker for disease severity and treatment effects.

Comments: This is an interesting study addressing the potential role of nerve US as a biomarker for Friedreich's ataxia. The good point is that the authors followed a standard scanning protocol, assessed multiple nerves, and scanned them along their entire courses. The limitations include small sample size and the lack of assessment of other sonographic parameters like nerve echogenicity and vascularity. Nerve US has become an important assessment tool in many NM disorders. Knowledge of its possible utilities help its integration in clinical practice.

Article of similar interest: Mulroy E, Pelosi L, Leadbetter R, et al. Peripheral nerve ultrasound in Friedreich ataxia. *Muscle Nerve*. 2018;57(5):852-856. doi:10.1002/mus.26012

August 7, 2024

Citation: Zheng Y, Hu J, Sun C, et al. Insights into refractory chronic inflammatory demyelinating polyneuropathy: A comprehensive real-world study. *Front Neurol.* 2024;15:1326874. Published 2024 Jan 31. doi:10.3389/fneur.2024.1326874

Submitted by: Nakul Katyal, MD
Edited by: Milvia Pleitez, MD

Summary: In this study, the authors sought to delineate the clinical characteristics, disease progression patterns, and potential risk factors associated with refractory chronic inflammatory demyelinating polyneuropathy (CIDP), as well as the electrophysiological features of this condition.

The authors applied the 2021 European Academy of Neurology/Peripheral Nerve Society (EAN/PNS) clinical criteria for CIDP to a cohort of neuropathy patients sourced from a national rare disease center database.

Treatment response was defined as an improvement confirmed objectively by either: (1) A minimum increase of 4 points on the Medical Research Council sum score, (2) A reduction of at least 1 point on the Inflammatory Neuropathy Cause and Treatment (INCAT) disability score, or (3) A decrease of at least 1 point on the modified Rankin Scale.

Refractory CIDP was characterized by: (1) Lack of response to at least two out of three initial treatment options (corticosteroids, intravenous immunoglobulin (IVIG), or therapeutic plasma exchange (TPE)) or relapse during tapering of medication; or (2) Dependence on at least two out of three initial treatment options simultaneously for maintaining treatment efficacy; or (3) No response to at least one out of three initial treatment options combined with the addition of an immunosuppressive drug (such as rituximab, azathioprine, mycophenolate mofetil, methotrexate, fingolimod, or cyclophosphamide).

Additionally, within the refractory CIDP subgroup, four distinct disease progression patterns were identified: relapsing–remitting, stable, secondary progressive, and primary progressive forms.

Among the 58 CIDP patients included, 33 were classified as having non-refractory CIDP while 25 were categorized as having refractory CIDP. Within the refractory CIDP group, 42.86% exhibited a relapsing–remitting pattern, 23.81% displayed a secondary progressive pattern, 23.81% maintained a stable course, and 14.29% presented with a primary progressive pattern.

According to the 2021 EAN/PNS guideline, among the refractory CIDP patients, 14 (56.0%) were diagnosed with typical CIDP, while 11 patients presented with CIDP variants (including 7 with distal CIDP, 1 with multifocal CIDP, 1 with focal CIDP, 1 with motor CIDP, and 1 with sensory CIDP).

In comparison to non-refractory CIDP patients, those with refractory CIDP exhibited longer disease duration (48.96 ± 33.72 vs. 28.33 ± 13.72 months) and more severe functional impairment as evidenced by both Medical Research Council sum score and INCAT disability score. Electrophysiological studies also indicated greater axonal impairment and more severe demyelination in refractory CIDP cases compared to non-refractory ones.

Motor nerve conduction studies revealed significantly lower ulnar compound muscle action potential, prolonged ulnar and median distal latency, reduced median conduction velocity, and prolonged F-wave latency in the refractory CIDP group compared to the non-refractory group. Additionally, sensory nerve conduction studies indicated a more pronounced reduction in conduction velocity on the ulnar nerve in refractory CIDP patients compared to their non-refractory counterparts. Disease duration emerged as an independent risk factor for refractory CIDP.

Comments: This study provided a comprehensive description of refractory CIDP, addressing its clinical features, classification of clinical course, electrophysiological characteristics, and prognostic factors.

The findings indicated that refractory CIDP patients exhibited a longer disease duration, more pronounced functional impairment, significant axonal damage, and more severe demyelination based on electrodiagnostic assessments.

A primary limitation of the study lies in its retrospective nature, small sample size, and reliance on data from a single center located in a region with restricted availability and accessibility issues regarding IVIG treatment. Refractory CIDP is a challenging subset of CIDP. It does not respond well to immune therapy and causes substantial disability. This study contributes to a better understanding of this challenging subset of CIDP and might be informative for management and treatment strategies.

Article of similar interest: Godil J, Barrett MJ, Ensrud E, Chahin N, Karam C. Refractory CIDP: clinical characteristics, antibodies and response to alternative treatment. *J Neurol Sci.* (2020) 418:117098. doi: 10.1016/j.jns.2020.117098.

Aug. 21, 2024

Citation: Kandemir O, Adar S, Dündar Ü, et al. Effectiveness of pulse electromagnetic field therapy in patients with subacromial impingement syndrome: A double-blind randomized sham controlled study. *Arch Phys Med Rehabil.* 2024;105(2):199-207. doi:10.1016/j.apmr.2023.09.020

Submitted by: Joshua M. Wilson, MD
Edited by: Rebecca O'Bryan, MD

Summary: Pulse electromagnetic fields (PEMF) has been shown to promote tenocyte and myoblast proliferation in vitro. It has been further found to be associated with short-term improvements in pain and function in individuals with knee osteoarthritis. The authors of this study investigated PEMF application in subacromial impingement syndrome (SIS) in conjunction with physical therapy.

In a double-blinded control study, 80 individuals with SIS symptoms or radiographic evidence of SIS were recruited from outpatient clinics. Study participants were randomized to the PEMF 5 days a week for 4 weeks or sham PEMF. All participants underwent standardized physical therapy for 4 weeks in the hospital under supervision. Visual analogue scale (VAS) pain scores, active joint range of motion (ROM), and muscle strength were recorded before and after 4 weeks and again at a 12 week follow up appointment. During evaluations functional capacity was assessed using the Constant Murley Score (CMS) and the Shoulder Pain and Disability Index (SPADI).

At baseline, the groups were similar in age, sex, and symptom duration. There were noticeable differences in favor of sham group having more shoulder flexion and internal rotation at baseline. While both groups had linear reductions in pain, the PEMF group had lower VAS scores at rest (0.17±0.50 vs 1.6±1.49, $p<0.001$) and with movement (0.90±1.46 vs 3.85±1.99, $p<0.001$). Despite the sham PEMF arm having greater ROM at baseline, the PEMF group achieved significantly more ROM gains and overall degree of ROM in shoulder flexion (139° to 177.92°±9.77 vs 152.97° to 175.72°±7.82; $p=0.002$) and resolution of differences in internal rotation (67.97°±16.88 to86.1°±7.19 vs 79.22°±11/57 to 86.90°±5.49; $p=0.876$). PEMF was associated improved function with lower total SPADI scores (5.48±9.72 vs 18.65±15.99; $p<0.001$) and higher CMS scores (90.42±6.94 vs 78.07±12.86; $p<0.001$).

Comments: Being a large double blinded randomized controlled trial, it provides compelling evidence for PEMF as adjunct to physical therapy for SIS. The outcome is clouded using weighted randomization for sex and age resulting in group differences at baseline. In addition, it would have been interesting to have a PEMF only group, to see if benefit was additive or synergistic with physical rehabilitation. It would also be valuable to have more long term follow up to see chance of reoccurrence and durability of response. SIS/rotator cuff pathology and their referred pain pattern are common mimics for cervical radiculopathy and axillary nerve injury. These are frequent reasons that patients are referred for electrodiagnostic evaluation. Patients and clinicians are often left disappointed when a very symptomatic individual is found to have a normal study and no diagnostic clarity. Knowledge of nerve injury mimics and available treatments are essential to producing well-round EDX physicians.

Articles of similar interest:

1. Liu M, Lee C, Laron D, et al. Role of pulsed electromagnetic fields (PEMF) on tenocytes and myoblasts-potential application for treating rotator cuff tears. *J Orthop Res.* 2017;35(5):956-964. doi:10.1002/jor.23278

2. Tong J, Chen Z, Sun G, et al. The efficacy of pulsed electromagnetic fields on pain, stiffness, and physical function in osteoarthritis: A systematic review and meta-analysis. *Pain Res Manag.* 2022;2022:9939891. Published 2022 May 9. doi:10.1155/2022/9939891

3. Sorrell RG, Muhlenfeld J, Moffett J, Stevens G, Kesten S. Evaluation of pulsed electromagnetic field therapy for the

treatment of chronic postoperative pain following lumbar surgery: a pilot, double-blind, randomized, sham-controlled clinical trial. *J Pain Res*. 2018;11:1209-1222. Published 2018 Jun 22. doi:10.2147/JPR.S164303

Sept. 4, 2024

Citation: Frutos-Reoyo EJ, López-Izquierdo R, Luque-Linero P, et al. Analysis of predictive factors for the poor prognosis of peripheral facial paralysis. *Am J Phys Med Rehabil.* 2024;103(3):245-250. doi:10.1097/PHM.0000000000002328

Submitted by: Nandita Keole, MD
Edited by: Milvia Pleitez, MD

Summary: The aim of the study is to evaluate predictive factors for a poor prognosis in patients with facial paralysis evaluated in the rehabilitation department of a tertiary hospital.

This prospective cohort study analyzed patients aged 18 years or older with a diagnosis of facial paralysis or facial paresis (lower motor neuron) who were seen in the emergency department of Río Hortega University Hospital in Valladolid, Spain, and referred for a Physical Medicine and Rehabilitation (PM&R) consultation during 2019. The severity of the condition was assessed using the House-Brackmann and Sunnybrook Facial Grading System (SFGS) scales at the first appointment (SFGS1) and at a follow-up appointment 1 month after symptom onset (SFGS2) in the PM&R service. The neurophysiological profile, determined through electrodiagnostic (EDX) testing (neurapraxia, axonotmesis, neurotmesis), was also analyzed as an independent variable. Patients were followed monthly for 6 months. Those who required elective botulinum toxin injections, surgical intervention, or follow-up beyond 6 months due to incomplete recovery were considered to have a poor prognosis. Descriptive and analytical analyses of clinical and epidemiological variables were conducted over the 6-month follow-up period.

A total of 47 adult patients were analyzed, 54.2% of whom were women. The mean age was 53.2 yrs. (SD, 15.5 yrs.). Twenty-five percent had an unfavorable prognosis. A statistically significant association with prognosis was observed for neurophysiological results and the scores of the House-Brackmann scale and the SFGS.

Neurophysiological tests are especially useful when evaluating prognosis. Likewise, SFGS is a useful and accessible tool with prognostic value, especially within a month of initial diagnosis, when a score lower than 65 indicates a poor prognosis with high sensitivity and specificity. These tools can be especially useful to reduce the clinical and psychological impact and to provide patients with early therapeutic management. A delay in performing aggressive techniques can lead to atrophy and irreversible fibrosis of the native musculature that makes many of the nerve resuscitation techniques useless.

Comments: In this study they did not specify whether they only reviewed idiopathic facial nerve palsy. This is useful to consider in places where EDX studies are not easily available. This study shows the prognostic value of the House-Brackmann and SFGS scales which could be used as an adjunct tool in clinic. Early intervention could help improve outcomes in patients who score lower (between 65 and 70 on the SFGS and those who stay at level II or higher on the House-Brackman scales).

Sept. 18, 2024

Citation: Aman IM, Zutshi K, Singla D. Dry needling versus corticosteroid injections to treat tendinopathy: A systematic review. *J Int Soc Phys Rehabil Med.* 2023;6(3):77-82. doi:10.1097/PH9.0000000000000014.

Submitted by: Sarah Breevoort, MD, PhD
Edited by: Rebecca O'Bryan, MD

Summary: This study is looking at the comparison of dry needling to steroid injection for treating tendinopathy.

During physical activities and exercise there is increased stress and force exerted on the tendon which increases the risk of both traumatic and overuse injury. Tendon injuries have become a common health issue and often is a musculoskeletal mimic that is commonly referred for electrodiagnostic testing. Dry needling can be used to treat muscles, tendons, and neuromuscular bundles and can lower central and peripheral sensitization by affecting substance P, endorphin, and local blood flow. Several studies suggest that dry needling has a positive influence in treating tendinopathies. Similarly, corticosteroid injections are used to treat tendon injuries, however, also have several disadvantages and risks.

In this systematic review the authors compare dry needling with steroid injections for tendinopathy and their efficacy in reducing symptoms.

The authors identified 121 articles which included dry needling or corticosteroid injections as their treatment protocol and any type of tendinopathy as a condition. Based on eligibility criteria ultimately four articles were selected for review. In these studies, dry needling versus single dose corticosteroid methylprednisolone acetate injections were compared and follow up was done at several weeks, months, and up to 1 year in one study. Outcome measures included visual analog scale, numerical pain rating scale and functional outcome measures to compare the effect of dry needling and steroid injection.

This systematic review of randomized control studies comparing dry needling with corticosteroid injection for the treatment of tendinopathy was limited by sample size, however, did find evidence of the effectiveness of both steroid injection and dry needling for the treatment of tendinopathy. From the selected data, authors conclude that both dry needling and corticosteroid injections are significantly better for short-term use, whereas dry needling is significantly better than corticosteroid for long-term use as there are no or less adverse effects of dry needling in comparison with corticosteroid injections.

Comments: Corticosteroid injection and dry needling have been widely used for the treatment of musculoskeletal conditions; however, it is unclear which intervention is the most effective. This study is one of a few recent systematic reviews that seeks to address this matter. This systematic review is a recent attempt to address the efficacy of in a head-to-head comparison of both dry needling and corticosteroid injections for the treatment of tendinopathy. The authors admit the limitation of small sample size of randomized controlled trials highlighting a potential opportunity for future studies. Both dry needling and corticosteroid injections are widely used for the treatment of tendinopathies, however, corticosteroid injections have more inherent risks, require more training or expertise for administration, and may not be as easily available understanding the comparative effectiveness has significant clinical utility. This review highlights the need for additional studies but does demonstrate the efficacy of dry needling for long-term treatment.

This article has relevance for the AANEM audience as many referrals for EDX studies are musculoskeletal mimics. Many tendinopathies present with pain at tendon insertion sites where common mononeuropathies also may cause discomfort. If EDX physicians or allied health staff could offer in clinic treatment that is both relatively safe and effective this could enhance patient care as well as increase provider satisfaction by being able to offer in lab treatment for study patients who often have normal EDX tests.

Articles of Similar Interest:

1. Sousa Filho LF, Barbosa Santos MM, Dos Santos GHF, da Silva Júnior WM. Corticosteroid injection or dry needling for musculoskeletal pain and disability? A systematic review and GRADE evidence synthesis. *Chiropr Man Therap*. 2021;29(1):49. Published 2021 Dec 2. doi:10.1186/s12998-021-00408-y

2. Stoychev V, Finestone AS, Kalichman L. Dry needling as a treatment modality for tendinopathy: A narrative review. *Curr Rev Musculoskelet Med*. 2020;13(1):133-140. doi:10.1007/s12178-020-09608-0

Oct. 2, 2024

Citation: Broers MC, Wieske L, Erdag E, et al. Clinical relevance of distinguishing autoimmune nodopathies from CIDP: Longitudinal assessment in a large cohort. *Journal of Neurology, Neurosurgery & Psychiatry* 2024;95:52-60.

Submitted by: Pritikanta Paul, MD
Edited by: Miliva Pleitez, MD

Summary: Patients with autoimmune nodopathy (AN) typically have specific clinical features and may not respond well to initial treatment with intravenous immunoglobulin (IVIg). However, there is limited documentation on investigating serial antibody titers in correlation with treatment response over the disease course.

This prospective study aimed to assess the treatment response in patients with AN initially diagnosed as chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). Antibody titers for neurofascin-155 (NF155), contactin-1 (CNTN1), and contactin-associated protein 1 (CASPR1) were measured in CIDP patients. Among 401 patients, 21 were identified with AN. The study's findings align with previously reported prevalence rates for anti-NF155 (3% vs 1–25%), anti-CNTN1 (2% vs 0.7–7%), and anti-CASPR1 (2% vs 0.2–3%) antibodies.

The study observed stable or increased antibody titers in most patients treated with IVIg. Patients undergoing plasmapheresis, corticosteroids, rituximab®, or a combination tended to experience a decrease in antibody titers. Notably, stopping immunomodulatory therapy led to clinical deterioration in four patients, accompanied by the reappearance of antibodies or an increased antibody titer in three cases supporting their pathogenic role. All four patients demonstrated clinical improvement upon resuming treatment. The authors concluded that monitoring disease activity using antibodies against paranodal proteins can be beneficial, particularly when contemplating treatment withdrawal. Limitations of the study include diverse treatment regimens among patients, complicating the assessment of treatment efficacy.

Comments: This study shows that patients with AN treated with plasma exchange, corticosteroids, or rituximab® often reduce antibody levels, but stopping therapy may cause clinical decline and antibody reappearance. This highlights the potential of using antibodies against nodal/paranodal proteins to monitor disease activity during treatment withdrawal. Further research is needed to compare rituximab's effects with non-B-cell depleting agents. A vast majority of AANEM audience are care providers for patients with CIDP and autoimmune nodopathy and this study provides updated knowledge as well as directions for future research.

Oct. 16, 2024

Citation: Granger A, Rajnauth T, Lahoria R, et al. Clinicopathologic findings in patients with paraneoplastic neuropathies and antibodies strongly associated with cancer. *Neurology*. 2024;102(2):e207982. doi:10.1212/WNL.0000000000207982

Submitted by: Milvia Y. Pleitez, MD
Edited by: Rebecca O'Bryan, MD

Summary: This is a retrospective review of the electronic medical record over a 27-year period of patients with paraneoplastic neurological syndromes (antibody positive) and clinicopathological findings on nerve biopsies. A total of 19 patients were identified to have paraneoplastic antibodies and included those that were positive for Amphyiphysin (4 patients), ANNA-1 (6 patients), ANNA-1 and CRMP 5 (3 patients), ANNA-2 (2 patients), and CRMP-5 (4 patients) were included. Neuropathy phenotypes noted were sensorimotor peripheral neuropathy (6), sensory neuropathy (3), lumbosacral radiculoplexus neuropathy (3), polyradiculopathy (2), and multifocal sensorimotor neuropathy (2). Nerve biopsies all showed axonal degeneration with three showing a mixed axonal and demyelinating type of neuropathy. Three nerve biopsies were normal. All biopsies showed reduced nerve fiber density with 16/19 showing subperineural edema. Epineural/perivascular inflammation was found in three.

These findings suggest that patients with sensorimotor and sensory neuropathies, especially if subacute, should be considered for paraneoplastic antibody testing. Additionally, patients who have reduced nerve fiber density, absent inflammation and subperineurial edema on nerve biopsy should also undergo paraneoplastic antibody testing.

Comments: This study is limited by it being retrospective and regional. However, it points out the importance of thinking about paraneoplastic causes for neuropathy especially in sensory peripheral neuropathies. This study will help clinicians recognize the importance of thinking about paraneoplastic etiologies for sensory neuropathies and in cases when nerve biopsies have the triad of reduced nerve fiber density, absent inflammation and subperineurial edema.

Oct. 30, 2024

Citation: Owusu R, Savarese M. Long-read sequencing improves diagnostic rate in neuromuscular disorders. *Acta Myol.* 2023;42(4):123-128. Published 2023 Dec 20. doi:10.36185/2532-1900-394

Submitted by: Justin Willer, MD
Edited by: Milvia Pleitez, MD

Summary: Short read sequencing has limitations including inaccurate genome assembly, an inability to detect large structural variants and variants in hard to sequence areas, such as highly repetitive sequences.

Long read sequencing reads DNA from 1,000 bases to several kilobases. It can detect large and small structural variants, repeat expansions and epigenetic modifications, such as DNA methylation. It eliminates bias associated with DNA amplification as single DNA molecules can be sequenced and increases accuracy and reduces the time need for the molecular diagnosis of NM disorders. It has been successful in detecting novel rare structural variants particular in the Duchenne muscular dystrophy (DMD) gene in patients with DMD.

It has also been used for diagnosing patients with oculopharyngeal MD after short read sequencing failed to find a pathogenic variant. It has also been used to identify C4Z4 repeats in Facioscapulohumeral muscular dystrophy (FSHD). It has also been helpful in diagnosing repeat expansions in Myotonic dystrophy type 1.

Long read sequencing has also been used for haplotyping in spinal muscular atrophy and allowed the detection of silent carriers and helped identify inheritance patterns of survival motor neuron (SMN) 1 and SMN2 haplotypes in most of the families of silent carriers.

Comments: A powerful new tool for the molecular diagnosis of NM disorders.

Nov. 13, 2024

Citation: Berger MJ, Dengler J, Westman A, et al. Nerve transfer after cervical spinal cord injury: Who has a "Time sensitive" injury based on electrodiagnostic findings? *Arch Phys Med Rehabil.* 2024;105(4):682-689. doi:10.1016/j.apmr.2023.11.003

Submitted by: Josh Wilson, MD
Edited by: Nakul Katyal, MD

Summary: Injuries sustained during a traumatic spinal cord injury (tSCI) are pure (central nervous system) CNS lesions and many have evidence of lower motor neuron lesion (LMNL). During the care of these individuals, LMNL may go undetected during early to subacute management. Individuals that sustain significant denervation of intrinsic hand muscle may miss the ideal opportunity for early nerve transfer and thereby potentially reducing their chances for improved outcome. While the literature has demonstrated good outcomes after 1 year of injury, clinically 6 months is often used as the ideal time in which to complete a nerve transfer. This study investigated the use of nerve conduction studies (NCSs) to investigate the degree of injury and change overtime to help identify the subpopulation of tSCI that would best be served by early consideration of nerve transfer.

In a retrospective review of records using the European Multicenter Study About SCI database, 79 individuals with tSCI underwent formal NCS evaluation at 3 and 6 month injury and completed standardized muscle testing using the Medical Research Council score. An independent limb analysis was conducted to account for individual heterogeneity, resulting in a total of 145 limbs analyzed. Only individuals with a score of four or higher at the C5-6 level and partial innervation of intrinsic hand muscles with a grade below three were included in the review. The ulnar motor compound motor action potential (CMAP) amplitude was utilized as a surrogate for C8-T1 spinal levels and results were categorized into normal (>6.0 mV), sub-normal (1.0-5.9 mV), and very abnormal (<1.0 mV).

At baseline, 74.7% of subjects had American Spinal Injury Association (ASIA) Impairment Scale scores of A or B. At 3 months, 87.2% had CMAP that were either subnormal or very abnormal, which decreased to 80% at 6 months. Over the 3 month period, only four limbs (9.1%) improved at all, and none reached normal range. Twelve of the limbs (16%) improved to normal level. Comparing complete versus incomplete tSCI, there was no difference in CMAP amplitude ($p=0.31$). However, incomplete tSCI showed a median CMAP that was 2.4 mV greater than incomplete injuries ($p=.001$). Utilization of a CMAP amplitude cut off of <1.0 mV resulted in a positive predictive value of 0.73 and 0.78 for muscle strength of zero versus 1-2 for C8 and T1 segments respectively.

Comments: Following tSCI there exists a subpopulation of individuals who are unlikely to regain functional hand use and are also amenable to nerve transfers. Individuals with damage resulting significantly in the denervation of intrinsic hand muscle, in essence, have a finite time before atrophy and fibrosis makes successful nerve transfer unlikely. While ulnar CMAP amplitudes are often tolerable of axonal loss up to 50%, the result of this study provides an objective cut off for clinicians to identify at-risk individuals in a timely manner. It also provides a 3-month time period for clinicians to provide stabilizing care and for confirmation of LMN findings, but also a significant amount of time in which individuals can be evaluated as surgical candidates. Traumatic SCIs are rarely just injuries of the SCI and there often exist concurrent peripheral nerve injuries. Providers rely on the expertise and clinical knowledge of EDX physicians in evaluating and fully characterizing these injuries. The insights gained from this study can assist clinicians in managing and improving outcomes for patients with SCI, while also drawing attention to potentially overlooked peripheral nerve injuries.

Nov. 27, 2024

Citation: Jabari, D., Heim, A., Ciersdorff, A., Wilkins, H., Agbas, A., Kosa, E., Hunt, S., Pasnoor, M., Dimachkie, M., & Barohn, R. (2024). Safety and tolerability of phenylbutyrate in inclusion body myositis. *RRNMF Neuromuscular Journal*, 5(1).

Submitted by: Sarah Breevoort, MD
Edited by: Nandita Keole, MD

Summary: This is a pilot study that demonstrates the safety and tolerability of phenylbutyrate (PBA) for the treatment of inclusion body myositis (IBM). IBM is the most common acquired muscle disorder in individuals over the age of 50. IBM was classically defined as an inflammatory myopathy based on inflammatory infiltrates found on muscle biopsy. The lack of response to treatment, however, raised concerns that IBM is a degenerative disorder with secondary inflammation. The abnormal accumulation of amyloid-beta protein precursor and its proteolytic fragment amyloid-beta is thought to be the key pathogenic event. Amyloid-beta oligomers, which are highly cytotoxic, have been demonstrated in IBM muscle tissues. Many neurodegenerative disorders are characterized by the accumulation of intracellular and extracellular protein aggregates that act to catalyze downstream processes that result in additional aggregation of proteins. A highly conserved class of proteins called molecular chaperones have evolved to prevent inappropriate interactions between polypeptides, enhance efficiency of protein folding and promote refolding repair of proteins. PBA, an orally active chemical chaperone approved by the FDA for the treatment of urea cycle disorders, mimics the function of intracellular molecular chaperones. Recent studies reported a novel function for PBA in cultured human muscle fibers that resulted in improved lysosomal activity and ameliorated impaired autophagy, providing a rationale for considering PBA for the treatment of IBM. This is a single-site phase I pilot study. Ten patients with sporadic IBM were enrolled, and following a 3-month run in period, treated with PBA for 3 months. All 10 subjects completed the study, and PBA was well tolerated with no serious adverse events. The most common adverse events were gastrointestinal-related and did not require stopping treatment. One of the biomarkers (MitoTracker™) showed a statistically significant drop over the treatment period. There was no statistically significant change in other secondary outcome measures (multiple strength and functional measures), but the study was limited by small sample size and short treatment period.

Comments: While limited by small sample size and short treatment period, the group met their primary endpoint of demonstrating safety and tolerability of PBA. This chemical chaperone already is FDA approved for the treatment of urea cycle disorders and has demonstrated in pre-clinical models the ability to restore the cellular homeostasis that is disrupted in cultured human muscle fibers with experimentally inhibited autophagy and lysosomal activity. It is believed that the pathogenesis responsible for the degenerative process that results in IBM is due to these disrupted processes. As PBA is already FDA approved and in this study has demonstrated safety and tolerability in patients with IBM, it is a rationale potential therapeutic option and warrants further study. Additional studies looking at secondary functional measures following earlier initiation during disease course with longer follow up period will be insightful.

Dec. 11, 2024

Citation: Allen J, Stone-Ghariani A, Quezada G, et al. Living with dysphagia: A survey exploring the experiences of adults living with neuromuscular disease and their caregivers in the United Kingdom. *J Neuromuscul Dis*. 2024;11(2):389-410. doi:10.3233/JND-230002

Submitted by: Pritikanta Paul, MD
Edited by: Nakul Katyal, MD

Summary: Dysphagia is prevalent in adults with neuromuscular disease (NMD), leading to complications like malnutrition and pneumonia, impacting quality of life. Challenges in healthcare delivery highlight the need for patient-centered dysphagia management pathways and research.

This cross-sectional study used surveys to explore dysphagia experiences in NMDs. One survey targeted individuals with NMDs, featuring 40 mostly multiple-choice questions covering various aspects of their condition. Another survey, with 43 questions, focused on caregivers who had cared for someone with NMD and swallowing issues in the past 18 months. Participants and caregivers aged 18 years or older, self-screened for eligibility and completed the surveys online.

A total of 555 responses were received, with 248 surveys excluded due to incomplete data. The remaining 310 surveys included 272 from individuals living with NMD and 38 from caregivers.

The survey findings across various NMD groups revealed a consistent challenge with swallowing solids compared to liquids, consistent with existing research on dysphagia in NMD. However, they also highlighted distinct variations in symptom prevalence among these groups, underscoring the unique characteristics, severity, and progression of dysphagia within each disease category, as documented in prior studies. Salient findings included patients with spinal muscular atrophy (SMA) reported longer mealtimes, possibly due to broader NM impairments affecting hand and arm function, complicating self-feeding. Respiratory muscle weaknesses in SMA may increase choking risks, while cognitive deficits in conditions like myotonic dystrophy type 1 (DM1) influence dysphagia perception and management. Authors suggest tailored dysphagia assessments are crucial to meet the diverse needs of each NMD group, suggesting a need for categorization based on underlying conditions.

Forty percent of participants with NM dysphagia lacked healthcare input, attributed to factors like prioritization of other health issues, patient self-management choices, and low awareness of dysphagia's impact. Among those who received healthcare, proactive assessment varied significantly between disease groups, with higher rates in DM1 (57.1%) compared to SMA (5.3%).

Additional findings included anxiety and caregiver concern regarding dysphagia are pronounced (3 times more than patients), with caregivers of individuals with DM1 and SMA showing heightened anxiety levels. The authors share that caregiver burden, influenced by the challenges of chronic disease care, emphasizes the need for comprehensive dysphagia assessments that consider both physical and psychological impacts.

In summary, adults with NMD receive insufficient information about potential swallowing difficulties before experiencing them. Both adults with NMDs and their caregivers desire earlier access to specialists and training to better manage swallowing difficulties.

The authors acknowledge limitations such as potential recall bias and survey response bias, which might lead to an overestimation of dysphagia's impact. Additionally, incomplete survey data and low representation from certain NMD groups may affect the study's generalizability and depth of insights.

Comments: The study highlights the profound impact of dysphagia on individuals with NMDs and their caregivers, emphasizing significant gaps in healthcare assessment and education. It reveals that a substantial number of NM patients experiencing dysphagia symptoms have not received professional evaluation, underscoring the need for improved healthcare

access and proactive management strategies. While dysphagia symptoms share commonalities across NMD groups, there are unique aspects specific to each disease, necessitating tailored approaches.

This article underscores the importance for the AANEM audience to recognize and manage dysphagia promptly and effectively in patients with NMDs. It highlights the critical role of healthcare providers in improving patient outcomes and supporting caregivers faced with dysphagia-related challenges.

Dec. 23, 2024

Citation: Oorschot S, Voorn E, Van Groenestijn A, Nollet F, Brehm M. Physical strain of walking in people with neuromuscular diseases is high and relates to step activity in daily life. *J Rehabil Med.* 2024;56:jrm40026. Published 2024 Jun 7. doi:10.2340/jrm.v56.40026

Submitted by: Rebecca O'Bryan, MD
Edited by: Nandita Keole, MD

Summary: The goal of the study was to determine the physical strain of walking based on actual measured oxygen consumption during walking (VO2walk) and peak oxygen consumption (VO2peak) in individuals with neuromuscular disease (NMD), and to assess the relationship between daily physical activity, expressed as daily step count and time spent in moderate to vigorous physical activity (MVPA), and physical strain of walking. Recruited from I'M FINE study in the Netherlands, inclusion criteria: Main inclusion criteria were: Diagnosed with Charcot-Marie-Tooth disease, post-polio syndrome, or other slowly progressive NMD; aged ≥ 18 years; and motivated to follow a physical activity programmed to improve aerobic capacity. Participants were excluded if they had contraindications for physical activity according to the American College of Sports Medicine guidelines; were unable to follow verbal or written instructions; had insufficient understanding of the Dutch language; or had participated in an exercise program for more than 4 weeks in the past 6 months. Only ambulatory participants with complete and valid baseline data for all variables of interest, as defined below, were included in the analyses of the current study. Manual muscle testing was performed. A walking energy cost test at a comfortable speed to assess VO2walk and walking speed, then an incremental increase in exercise to assess VO2peak, were performed. Daily physical activity during walking hours was measured for 7 consecutive days. This was measured using an accelerometer and a heart rate belt. Sixty-one subjects enrolled from the I'M FINE study completed the study. Analysis showed an inverse relationship between daily step count and physical strain of walking. No association between MVPA and physical strain of walking. NMD patients with high physical strain took fewer steps per day. However, time spent in MVPA was not related to physical strain of walking, which may indicate that despite a reduction in step count, strenuous daily activities are still being performed.

Overall, the study showed that physical strain of comfortable walking was severely increased in NMD. The physical strain was 73%, compared to 34-49% of able-bodied individuals. High physical strain of walking was associated with lower steps taken, while intensity of daily activity was not related. Authors suggest reducing VO2peak with aerobic exercise and potentially reducing VO2walk with lower limb orthoses as possible clinical applications.

Comments: This article is an interesting view into the day-to-day challenges of ambulatory patients with NMD. The physical challenges experienced in walking impacts daily step count but does not seem to be related to strenuous physical activity in general. Clinical implications highlighting the importance of aerobic capacity and optimizing durable medical equipment is an important observation. This article is a very applicable set of findings for those of us treating patients with NMD who are ambulatory in order to support their goals and needs as relates to community engagement and physical fitness. I think this solidifies what most of us already know – our patients have to work harder to do their normal daily activities, and still strive to do as much as they can given their limitations.


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